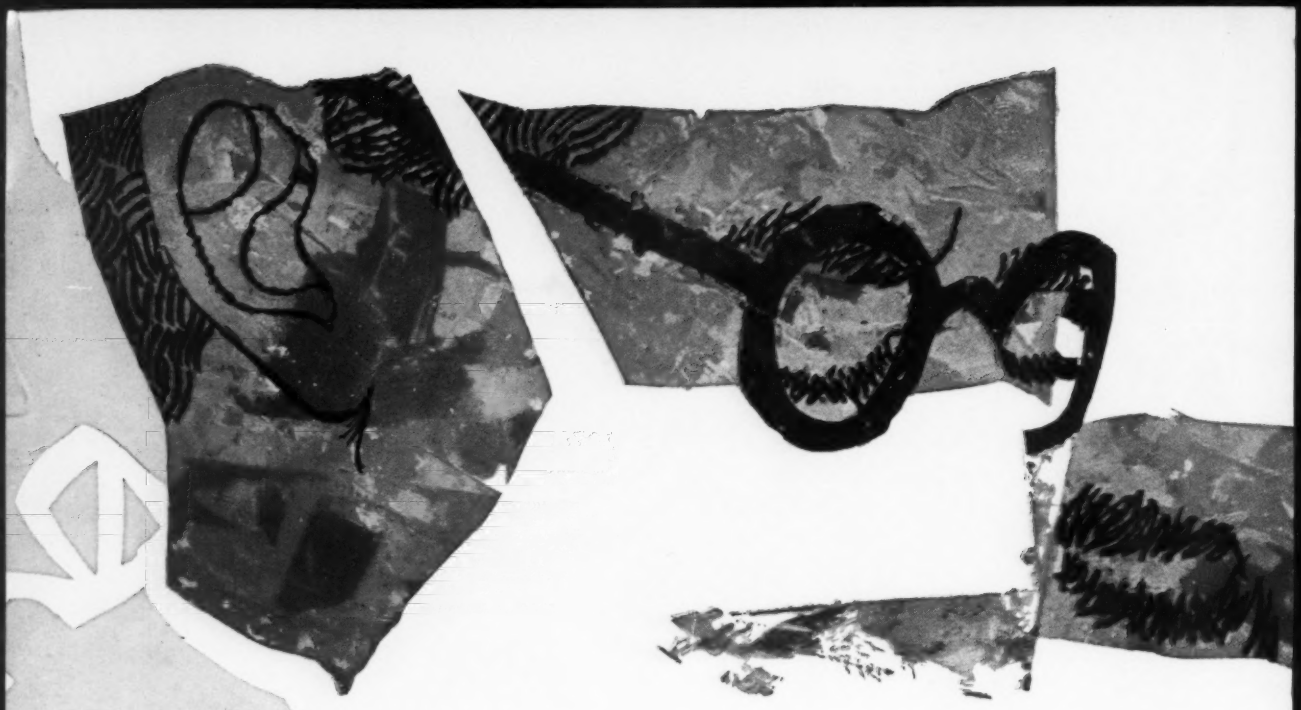
Delaware Medical Journal

ESTABLISHED 1776 — INCORPORATED 1789

Official Publication of the Medical Society of Delaware

JULY, 1961 ....

DELAWARE HOSPITAL ISSUE



inside as well as outside the hospital...
staphylococci usually remain sensitive to

CHLOROMYCETIN®

(chloramphenicol, Parke-Davis)

That the sensitivity patterns of "street" staphylococci differ widely from those of "hospital" staphylococci is a well-established clinical fact.[1-5] Although strains of staphylococci encountered in general practice have remained relatively sensitive to a number of antibiotics,[6] the problem of antibiotic-resistant staphylococci appears to be a threat to all patients in hospitals today. It is encouraging to note, however, "...that a relatively small percentage of strains develop resistance to chloramphenicol, despite the consumption of large amounts of this antibiotic."[7]

In one hospital, for example, CHLOROMYCETIN "...was the only widely used antibiotic to which few of the strains were resistant."[8] In another hospital, despite steadily increasing use of CHLOROMYCETIN since 1956, "...the percentage of chloramphenicol-resistant strains has actually been lower in subsequent years."[1] Elsewhere, insofar as hospital staphylococci are concerned, it appears that "...the problem of antibiotic resistance can be regarded as minimal for chloramphenicol."[2]

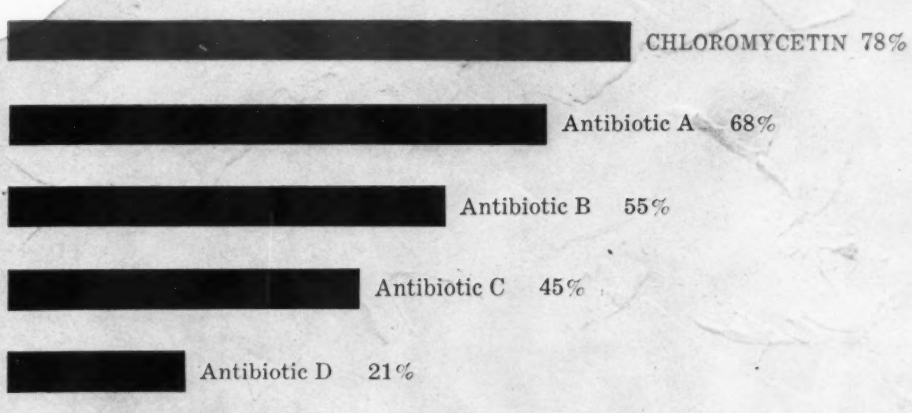
CHLOROMYCETIN (chloramphenicol, Parke-Davis) is available in various forms, including Kapseals® of 250 mg., in bottles of 16 and 100.

See package insert for details of administration and dosage.

Warning: **Serious and even fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, granulocytopenia) are known to occur after the administration of chloramphenicol. Blood dyscrasias have occurred after short-term and with prolonged therapy with this drug. Bearing in mind the possibility that such reactions may occur, chloramphenicol should be used only for serious infections caused by organisms which are susceptible to its antibacterial effects. Chloramphenicol should not be used when other less potentially dangerous agents will be effective, or in the treatment of trivial infections such as colds, influenza, viral infections of the throat, or as a prophylactic agent.**

Precautions: **It is essential that adequate blood studies be made during treatment with the drug. While blood studies may detect early peripheral blood changes such as leukopenia or granulocytopenia, before they become irreversible, such studies cannot be relied upon to detect bone marrow depression prior to development of aplastic anemia.**

IN VITRO SENSITIVITY OF 250 STRAINS OF STAPHYLOCOCCI TO CHLOROMYCETIN AND TO FOUR OTHER ANTIBIOTICS*



These strains of coagulase-positive staphylococci were isolated from hospitalized patients at a large county hospital during the year 1959. Sensitivity tests were done by the disc method.

*Adapted from Bauer, Perry, & Kirby[1]

References: (1) Bauer, A. W.; Perry, D. M., & Kirby, W. M. M.: *J.A.M.A.* 173:475, 1960. (2) Fisher, M. W.: *Arch. Int. Med.* 105:413, 1960. (3) Cohen, S.: *Circulation* 20:96, 1959. (4) Edwards, T. S.: *Am. J. Ophth.* 48, Part II:19, 1959. (5) Smith, I. M.: Staphylococcal Infections, Chicago, The Year Book Publishers, Inc., 1958, p. 148. (6) Petersdorf, R. G.; Rose, M. C.; Minchew, H. B.; Keene, W. R., & Bennett, I. L., Jr.: *Arch. Int. Med.* 105:398, 1960. (7) Editorial: *J.A.M.A.* 173:544, 1960. (8) Finland, M.; Jones, W. F., Jr., & Bennett, I. L., Jr.: *Arch. Int. Med.* 104:365, 1959.

51461

PARKE-DAVIS

PARKE, DAVIS & COMPANY, Detroit 32, Michigan

FOUNDED 1770
MEDICAL SOCIETY OF DELAWARE
INCORPORATED 1789

Delaware Medical Journal

Official Publication of the Medical Society of Delaware

EDITORIAL AND BUSINESS OFFICES
1925 LOVERING AVENUE, WILMINGTON 6, DELAWARE

VOLUME 33 **JULY, 1961** **NUMBER 7**

Owned and published by the Medical Society of Delaware, a scientific non-profit corporation.

Issued the fifteenth of each month under the supervision of the Committee on Publication.

CONTENTS

Entered as second-class matter June 28, 1929, at the Post Office at Wilmington, Delaware, under the Act of March 3, 1879.
Issued monthly.

A Vacation from Hay Fever is a Real Vacation

ANYWHERE – ANYTIME

Just a "poof" of fine **NTZ** *spray brings relief* IN SECONDS, FOR HOURS

NTZ is a potentiated, balanced combination of these well known synergistic compounds:

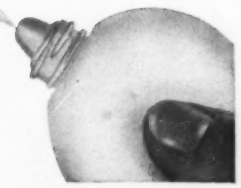
Neo-Synephrine® HCl, 0.5%
– dependable vasoconstrictor and decongestant.

Thenfadil® HCl, 0.1%
– potent topical antihistaminic.

Zephiran® Cl, 1:5000
– antibacterial wetting agent and preservative.

NTZ® NASAL SPRAY

Supplied in leakproof, pocket size squeeze bottles of 20 cc.



Winthrop LABORATORIES
New York 18, N.Y.

Put your low-back patient back on the payroll

Soma relieves stiffness —stops pain, too

YOUR CONCERN: Rapid relief from pain for your patient. Get him back to his normal activity, fast!

HOW SOMA HELPS: Soma provides direct pain relief while it relaxes muscle spasm.

YOUR RESULTS: With pain relieved, stiffness gone, your patient is soon restored to full activity—often in days instead of weeks.

> Kestler reports in controlled study: *Average time for restoring patients to full activity: with Soma, 11.5 days; without Soma, 41 days.* (*J.A.M.A. Vol. 172, No. 18, April 30, 1960.*)

Soma is notably safe. Side effects are rare. Drowsiness may occur, but usually only in higher dosages. Soma is available in 350 mg. tablets. **USUAL DOSAGE: 1 TABLET Q.I.D.**

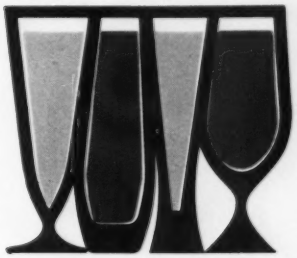
The muscle relaxant with an independent pain-relieving action

SOMA®

(carisoprodol, Wallace)

Wallace Laboratories, Cranbury, New Jersey

introducing...nutritional support in convenient, tasty, liquid form to supplement inadequate diets... to replace skipped meals



Nutrament T.M.

BRAND

nutritionally complete food

a nutritious meal, ready to drink

nutritional support is often needed for:

careless or irregular eaters—who skip breakfast or lunch or do not eat properly because of busy schedules or faulty eating habits.

children—who need increased basic nutrients during convalescence[1] or during difficult feeding periods, such as after tonsillectomies.[2]

adolescents—who require nutritional support because of growth needs and poor dietary selection.[3]

pregnant patients—who often require sound, easily tolerated, and convenient nutritional supplementation during pregnancy and lactation.[4]

geriatric patients and others—who cannot or will not maintain proper nutrition because of poor dentition, faulty eating habits, or lack of interest in eating.[5]

hospital patients—Nutrament liquid can serve as an excellent and convenient source of nourishment.

and in Oral, Dental or Surgical conditions—which interfere with or prevent consumption of solid food.

readily accepted by patients

Nutrament liquid requires no special preparation. Smooth texture and appealing taste of Nutrament make it readily acceptable. Equally delicious served hot or cold. Nutrament also has a high satiety value.

supplied

In 12½ fl. oz. cans, chocolate and vanilla flavors. Conveniently available at drug and food stores.

offers a scientifically balanced ratio of carbohydrate, protein, and fat. Each 12½ fl. oz. can of Nutrament liquid provides 400 calories. Caloric distribution: protein–20% (20 Gm.); carbohydrate–50% (50 Gm.); fat–30% (13.3 Gm.); plus the following vitamins and minerals:

		% MDR
Vitamin A (U.S.P. Units)	1250	30
Vitamin D (U.S.P. Units)	125	30
Vitamin C, mg.	50	166
Thiamine, mg.	0.5	50
Riboflavin, mg.	0.6	50
Niacinamide, mg.	5	50
Calcium, Gm.	0.5	67
Phosphorus, Gm.	0.4	53
Iron, mg.	4	40
Iodine, mcg.	60	60

Vitamin E (Int. Units)	2.5
Pyridoxine, mg.	0.4
Vitamin B_{12}, mcg.	0.5
Calcium pantothenate, mg.	2
Sodium, Gm.	0.2
Potassium, Gm.	0.9
Copper, mg.	0.5
Manganese, mg.	1
Fiber, Gm.	0.55

ingredients: Whole milk, skim milk, sugar, soy flour, Dextri-Maltose® (maltose and dextrins derived from enzymic action of choice barley malt on selected corn flour), starch, chondrus extract, sodium alginate, vitamin A palmitate, calciferol, sodium ascorbate, thiamine hydrochloride, niacinamide, ferrous sulfate, sodium iodide, *d*-alpha-tocopheryl acetate, pyridoxine hydrochloride, cyanocobalamin, calcium pantothenate, salt, cupric carbonate, manganese sulfate, cocoa and/or imitation vanilla flavor.

references: (1) Nelson, W. E.: Textbook of Pediatrics, ed. 7, Philadelphia, W. B. Saunders Company, pp. 231-233, 1959. (2) Parrott, R. H., and Nelson, W. E.: *ibid.*, p. 759. (3) Johnston, J. A.: Ann. New York Acad. Sc. *69*:881-901 (Jan. 10) 1958. (4) Burke, B. S., and Kirkwood, S. B., in Greenhill, J. P.: Obstetrics, ed. 12, Philadelphia, W. B. Saunders Company, 1960, pp. 126-131. (5) Skillman, T. G.; Hamwi, G. J., and May, C.: Geriatrics *15*:464-472 (June) 1960.

5706I

Edward Dalton Co.
A DIVISION OF
MEAD JOHNSON & COMPANY

Quality products from nutritional research

in bacterial tracheobronchitis

Panalba* promptly

to gain precious therapeutic hours

Panalba your broad-spectrum antibiotic of first resort

In the presence of bacterial infection, taking a culture to determine bacterial identity and sensitivity is desirable—but not always practical in terms of the time and facilities available.

A rational clinical alternative is to launch therapy at once with Panalba, the antibiotic that provides the best odds for success.

Panalba is effective (in vitro) against 30 common pathogens, including the ubiquitous staph. Use of Panalba *from the outset* (even pending laboratory results) can gain precious hours of effective antibiotic treatment.

Supplied: Capsules, each containing Panmycin* Phosphate (tetracycline phosphate complex), equivalent to 250 mg. tetracycline hydrochloride, and 125 mg. Albamycin,* as novobiocin sodium, in bottles of 16 and 100.

Usual Adult Dosage: 1 or 2 capsules 3 or 4 times a day.

Side Effects: Panmycin Phosphate has a very low order of toxicity comparable to that of the other tetracyclines and is well tolerated clinically. Side reactions to therapeutic use in patients are infrequent and consist principally of mild nausea and abdominal cramps.

Albamycin also has a relatively low order of toxicity. In a certain few patients, a yellow pigment has been found in the plasma. This pigment, apparently, a metabolic by-product of the drug, is not necessarily associated with abnormal liver function tests or liver enlargement.

Urticaria and maculopapular dermatitis, a few cases of leukopenia and agranulocytosis have been reported in patients treated with Albamycin. Most of these side effects usually disappear upon discontinuance of the drug.

Caution: Since the use of any antibiotic may result in overgrowth of nonsusceptible organisms, constant observation of the patient is essential. If new infections appear during therapy, appropriate measures should be taken.

Total and differential blood counts should be made routinely during prolonged administration of Albamycin. The possibility of liver damage should be considered if a yellow pigment, a metabolic by-product of Albamycin, appears in the plasma. Panalba should be discontinued if allergic reactions that are not readily controlled by antihistaminic agents develop.

*Trademark, Reg. U.S. Pat. Off.
The Upjohn Company
Kalamazoo, Michigan

Upjohn

75th year

for more satisfactory relief of anxiety-aggravated pain

PHENAPHEN®

- More satisfactory than "the usual analgesic compounds" for relieving pain and anxiety.[1]
- More effective than a standard A.P.C. preparation for relief of moderate to severe pain.[2]

Each PHENAPHEN *capsule contains:*

Acetylsalicylic acid (2½ gr.)	162 mg.
Phenacetin (3 gr.)	194 mg.
Phenobarbital (¼ gr.)	16.2 mg.
Hyoscyamine sulfate	0.031 mg.

Also available:

PHENAPHEN with CODEINE PHOSPHATE
¼ GR. (16.2 mg.) Phenaphen No. 2

PHENAPHEN with CODEINE PHOSPHATE
½ GR. (32.4 mg.) Phenaphen No. 3

PHENAPHEN with CODEINE PHOSPHATE
1 GR. (64.8 mg.) Phenaphen No. 4

Bottles of 100 and 500 capsules.

1. Meyers, G. B.: Ind. Med. & Surg. 26:3, 1957. 2. Murray, R. J.: N. Y. St. J. Med. 53:1867, 1953.

A. H. ROBINS CO., INC., RICHMOND 20, VIRGINIA
Making today's medicines with integrity... seeking tomorrow's with persistence.

Robins

Schering

"The experience to date with griseofulvin has been so promising for the management of *Microsporum audouini, Trichophyton tonsurans* and *Trichophyton violaceum* that it has become the treatment of choice for these infections of the scalp."[1]

oral **fulvicin**® griseofulvin

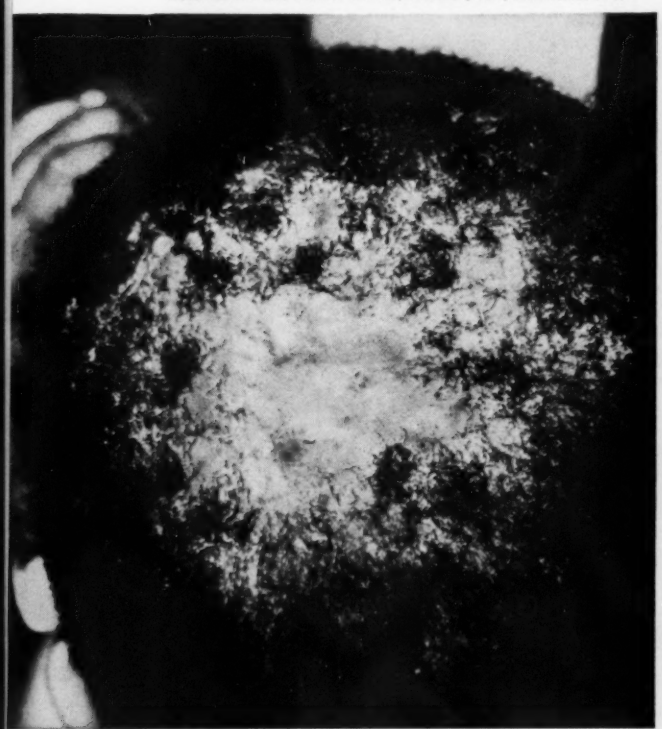
Supplied: FULVICIN Tablets (scored), 500 mg., in bottles of 20 and 100; 250 mg., in bottles of 30, 100 and 500. *Reference:* Sulzberger, M. B., *et al.:* Dermatology: Diagnosis and Treatment, ed. 2, Chicago, Year Book Publishers, 1961, p. 350. For complete details, consult latest Schering literature available from your Schering Representative or Medical Services Department, Schering Corporation, Bloomfield, N. J.

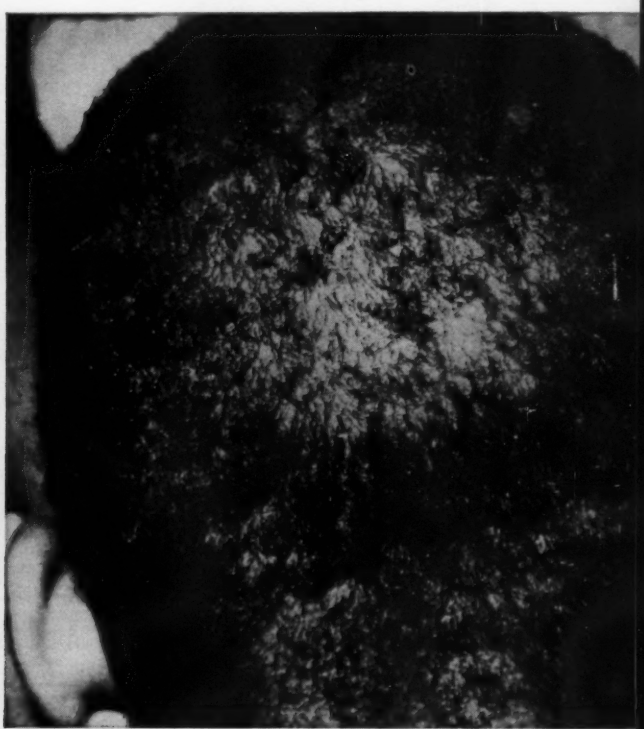
SCHERING CORPORATION • BLOOMFIELD, NEW JERSEY

S-826

***Tinea capitis due to* T. tonsurans *cleared after 7 weeks of therapy with* FULVICIN.**

FROM WEINER, M. A.; GOULD, A. H., AND GANT, J. O., JR.: GRISEOFULVIN IN RINGWORM INFECTIONS. SCIENTIFIC EXHIBIT PRESENTED AT A.M.A. CLINICAL MEETING, DECEMBER, 1960, WASHINGTON, D. C.





*New Product Announcement

Delaware Medical Journal

JULY, 1961
VOLUME 33
NUMBER 7

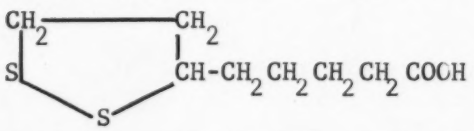
A SCREENING INVESTIGATION Of the Use of Lipoic Acid As an Anti-Diabetic Agent

• A clinical pilot experiment exploring the possible effects of lipoic acid in the diets of ten diabetic patients indicates that further study might be worthwhile.

LEWIS B. FLINN, M.D.
C. ANTHONY D'ALONZO, M.D.

Substances exhibiting the biological activity of alpha-lipoic acid were recognized in various laboratories, and an excellent review of these studies is available.[1,2] The duPont Company has developed a process to manufacture this substance synthetically. No conclusive evidence has appeared to prove that it might be of clinical value. Some of the laboratory findings and a few scattered clinical notations suggested it might lower blood sugar. In the spring of 1960 the Stine Laboratory of the duPont Company had a supply of lipoic acid on hand and suggested that we might be interested in investigating its possible clinical application.

The structural formula is as follows:



Dr. Flinn, F.A.C.P., Director, Department of Medicine and Chief of Metabolic Division, Delaware Hospital, is Governor for Delaware, American Diabetes Association.

Dr. D'Alonzo, F.A.C.P., is Assistant Director, Medical Department, duPont Company.

Dewey[3,4] and others did considerable pioneering work on this substance and concluded that it is a catalyst in the same area of metabolism as thiamine and coenzyme-A. This type of action suggests that only a small dose may be needed clinically to be effective. This catalytic activity was also pointed out in an article in Physiological Reviews in 1953 by Reed.[2,5] Alpha-lipoic acid seems to be involved as an acetate-replacing factor, as a protogen factor, and in the oxidation of pyruvate to acetate and CO_2. Altschule[6] and others have studied the effect of many substances in patients with schizophrenia. One of those substances studied was alpha-lipoic acid. No marked change occurred in the laboratory findings of patients to whom it was administered, but small doses seemed to result in clinical improvement, and larger doses aggravated the disorder. There were no side or toxic effects. Doses used were 40 milligrams intramuscularly or 100 milligrams by mouth, daily. When larger doses were used, such as 200 milligrams intramuscularly daily, the patients became

worse. As much as 50 milligrams has been given in a single dose intravenously by Turchetti,[7] without any toxic effect. It has been used with equivocal results in liver disease in the dosage of 20 milligrams twice a day intravenously by this same investigator. To a diabetic, Turchetti[7] gave 20 units of regular insulin along with 20 milligrams of lipoic acid intravenously, with a consequent lowering of the blood sugar at 2½ hours to 60 milligrams per cent.

Bornstein and Hartman[8] studied the effect of insulin on the glucose metabolism of liver slices and found that lipoic acid when added to the buffer, increased glucose oxidation.

Other unreported[9] studies on animals using much larger doses seemed to indicate that alpha-lipoic acid has a dramatic effect on carbohydrate metabolism in doses approaching 100 milligrams per kilogram of body weight given intramuscularly. Blood glucose is increased by such dosage in non-fasting animals and decreases in fasted animals. The difference is presumably due to release of glycogen in the non-fasted animals. Reduction of glucose in the fasted animals could be produced in the absence of the adrenal, hypophysis and the pancreas. Alpha-lipoic acid in this dosage, 100 milligrams per kilogram appeared to function independently of insulin. In this large dosage, body temperature may be markedly lowered. All these responses in high dosage occur in 4-6 hours. The toxic dose of alpha-lipoic acid thus far appears to be considerably higher than even these high doses used in the animal experiments, probably in the neighborhood of 200 milligrams per kilogram body weight intramuscularly. This is many times greater than the doses administered to clinical cases previously reported and in those reported here.

To explore the possible effects of lipoic acid in diabetic patients, we have studied ten patients as a clinical pilot experiment. Intravenous administration of the material might be more definitive in determining the effectiveness of the substance, but since this would not be a desirable method of administration for clinical use, the oral route was used entirely. It was given in capsule form. It was given to several individuals, diabetic and non-diabetic, and not included in this series, to determine if there were any side reactions or digestive difficulties. One patient complained of a burning sensation in the stomach after ingestion of the capsules. Aside from this there have been no complaints; no signs of any toxicity whatsoever. Because of the small dosage used and the short duration of treatment, no detailed blood or other laboratory examinations were made.

Case No. 1

Man, age 74, had had diabetes for five years. He was hospitalized, received a regular diet and, in addition, NPH insulin units 20 each morning and 50 mg. DBI. The average blood sugars, taken over a period of ten days, were: fasting 180 mg.%, and feasting: 204 mg.%. After 150 mg. per day of lipoic acid for three or four days and then 300 mg. a day for four days, fasting blood sugars varied from 94 to 116 mg.%, feasting blood sugars 164 to 88 mg.%. Lipoic acid was stopped for four days resulting in a fasting sugar of 108 mg.%, feasting sugar 224 mg.%. The insulin and DBI were stopped, lipoic acid only given, 300 mg. a day, and after five days fasting blood sugar 124 mg.%, feasting 149 mg.%. There was no glycosuria.

Case No. 2

Woman, age 41, diabetes eight years—NPH insulin 35 units; in the course of a week in the hospital fasting blood sugar averaged about 150 mg.%, feasting 160 mg.%. After receiving 300 mg. of lipoic acid daily for five days, the fasting blood sugar was 129 mg.%, and the feasting blood sugar was 144 mg.%. After stopping the lipoic acid for five days, the fasting blood sugar was 162 mg.%, and the feasting blood sugar was 137 mg.%. After five more days on 300 mg. of lipoic acid, the fasting blood sugar was 151 mg.% and the feasting 142 mg.%. No glycosuria was noted.

Case No. 3

Man, age 42, diabetic for fifteen years—marked neuropathy-hypoglycemic attacks. NPH reduced to 30 units, then to 15 units with DBI 75 mg. Blood sugars ranged from 62 to 85 mg.% fasting, and the feasting blood sugar was up to 300 mg.%. After receiving 900 mg. lipoic acid for three days along with 15 units NPH insulin, the feasting blood sugars ranged from 350 mg.% to 416 mg.% with 3 and 4 plus sugar in the urine.

Case No. 4

Woman, age 48, diabetes for ten years—NPH insulin 30 units, regulated diet in hospital, 3 to 4 plus glycosuria. Blood sugar, fasting 335 mg.%, fasting 280 mg.%. After eight days of lipoic acid 1500 mg. per day, with and without NPH insulin 50 units, and regular insulin 15 units, blood sugar and urine sugar unchanged. NPH 60 units, regular insulin 15 units, DBI 150 mg. a day, no lipoic acid—0 to 1 plus sugar in the urine, feasting blood sugar 160 mg.%.

Case No. 5

Man, age 40, diabetes ten years—on NPH insulin 30 units was sugar free, blood sugar 135 mg.%. After no insulin and lipoic acid 1500 mg. per day, blood sugar 160 mg.% and urine 3 plus. With no insulin and no lipoic acid but DBI 75 mg. a day, blood sugar was 145 mg.%, urine sugars 0 to 1 plus.

Case No. 6

Man, age 41, diabetes three years — never had had insulin—not well controlled on orinase. Chlorpropamide 500 mg. a day, blood sugar 280 mg.%, urine 3 to 4 plus. After four days of lipoic acid 1500 mg. a day, in addition to chlorpropamide 500 mg. per day, there was no change in blood sugars. On NPH insulin 25 units daily and 500 mg. of DBI, urine sugars were 0 to 1 plus, and blood sugar 150 to 160 mg.% feasting.

Case No. 7

Woman, age 51, diabetes five years—no insulin. Orinase 1.5 gm. daily, blood sugar 125 to 180 mg.%, urine varied from 0 to 3 plus sugar. After stopping orinase and taking lipoic acid 1500 mg. a day, blood sugar varied from 140 to 175 mg.% feasting, and urine varied from 0 to 4 plus.

Case No. 8

Woman, age 27, new patient, no insulin, no diet—blood sugar 253 mg.%, 1 to 2 plus sugar in the urine. Lipoic acid 300 to 1200 mg. a day, blood sugar 117 to 172 mg.%, some glycosuria.

Case No. 9

Man, age 55, new, no dietetic control or therapy, no insulin or other hypoglycemic agents—blood sugar 173 mg.%, 2 plus sugar in the urine. Lipoic acid 1500 mg. a day, blood sugar 134 mg.%. Glycosuria noted occasionally. Question arises as to whether this improvement is due to lipoic acid or voluntary change in diet.

Case No. 10

Man, age 67, recent diabetes, mild — blood sugars ranged 119 to 240 mg.%, mostly feasting. No glycosuria. Orinase 500 mg. twice a day. Glucose tolerance test—fasting 119, ½ hour 188, 1 hour 224, 2 hours 240, 3 hours 246. After three days of 300 mg. of lipoic acid and 500 mg. of orinase twice a day, glucose tolerance test was repeated—results—fasting 96, 1 hour 216, 2 hours 212, 3 hours 204; urine negative.

Comment

Lipoic acid may have had some slight beneficial effect in Case No. 1, a questionable effect in Case No. 2, a questionable effect in Case No. 9. The slight improvement in Case No. 10 in the glucose tolerance test after lipoic acid therapy is not considered to be significant.

The age of the patients studied ranged from 41 years to 74 years. Duration of diabetes varied from newly discovered untreated cases (two) to 15 years. Five cases had been taking insulin, one had been receiving chlorpropamide, two orinase and two untreated. One was a brittle diabetic with neuropathy. Lipoic acid was ineffective in preventing hypoglycemic attacks.

Six were mild cases, two moderately severe, two mild and new. All of the eight more difficult cases were subsequently satisfactorily controlled by diet and insulin with or without a hypoglycemic agent other than lipoic acid.

Conclusion

In the ten cases of diabetes summarized above in which lipoic acid was administered, there was no appreciable beneficial effect. Also, there were no obvious deleterious effects and no toxic side reactions. It is possible that in larger dosage better results might be obtained. Further study might be worthwhile, if conducted on a larger group of mild diabetics who had been followed on diet alone for a period of time before receiving lipoic acid. It might be worthwhile also to evaluate short term effects of intravenously administered lipoic acid on the blood sugar.

REFERENCES

1. Gunsalus, I. C.: The Chemistry and Function of P.O.F. (Lipoic Acid) Journal Cellular Comparative Physiology, 41: Supplement, 113, 1953.
2. Reed, L. J.: The Chemistry and Function of Lipoic Acid, advances in enzymology, New York, Interscience Publishers, 18, 319-347, 1957.
3. Dewey, V. C., Kidder, G. W., Fuirard, B. M., Smell, E. E., Reed, L. J., De Burk, B. G., Williams, R. J. O'Kane, D. J., Gunsalus, I. C.: Nutrition Reviews, 11, 2: 59-61, 1953.
4. Ibid. 15, 4: 109-111, 1957.
5. Reed, L. J.: Metabolic Functions of Thiamine and Lipoic Acid, Physiol. Reviews, 33, 544-545, 1953.
6. Altscule, M. D., Goncz, Rose-Marie, and Holliday, P. D.: Carbohydrate Metabolism in Brain Disease, XI, Effects of Thioctic (Alpha-Lipoic) Acid in Chronic Schizophrenia, Arch. Int. Med., 103, 726-729, 1959.
7. Turchetti, A.: Discussione, Atti del Simposio Internazionale su l'Acido Tioctico, Institute de Farmacologia del l'Universita' di Napoli, XI, Napoli, 28-29, 2811283, 1955.
8. Bornstein, J., and Hartman, B. D.: Effect of Thioctic Acid on Glucose Oxidation by Liver Slices, Nature, 176, 4486, 788-789, 1955.
9. Personal communication to authors. (Members of Stine Lab., E. I. duPont & Co.

New Members

Kurt Anstreicher, M.D., University of Vienna Medical College, '29, is an Austrian by birth and obtained his Delaware license in 1960. Specialty: Psychiatry. Dr. Anstreicher enjoys listening to his fine collection of music for relaxation, pursues the study of astronomy in his spare time and likes a good game of chess. Office: Delaware State Hospital, Farnhurst.

George D. MacEwen, M.D., is a Canadian by birth and received his medical training at University of Ontario. He came to this country in '53 and was in Washington, D.C., for two years prior to settling in this region. The MacEwens have three daughters and a son. Specialty: Orthopedic Surgery; Delaware license, 1960. Office: A. I. duPont Institute, Wilmington.

Joyce A. Z. Pearson, M.D., is a graduate of the Johns Hopkins School of Medicine, Baltimore; Delaware license: 1959. Dr. Pearson has two children and weekends are usually spent visiting both sets of grandparents in nearby Pennsylvania. Gardening is her hobby. Office: 4th & Franklin Streets, Wilmington. Specialty: General Practice.

Lloyd B. Harrison, M.D., University of Virginia, '45, was born in Greenwood, S.C. Dr. Harrison likes spectator sports such as baseball but prefers reading as a pastime. There are six children in the family. Specialty: Otolaryngology. Office: Professional Building, Wilmington.

GALLSTONE IMPACTED IN DUODENAL BULB

Report Of An Unusual Case

LEONARD ROSENBAUM, M.D.
CARL I. GLASSMAN, M.D.
JOHN W. ALDEN, M.D.

The occurrence of a gall stone impacted in the duodenal bulb following cholecystoduodenal fistula is rare even though about fifty percent of fistulae between the gallbladder and intestinal tract occur in the doudenum.[2] Only eight cases demonstrated roentgenologically have been reported.[1,3] The following is an additional case.

Case Report

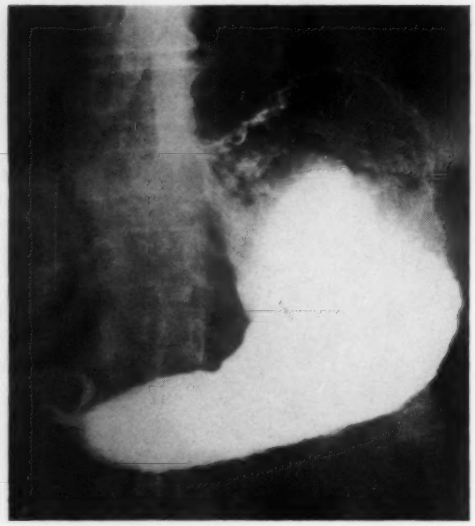
A 69 year old white widow, was admitted to the Delaware Hospital on September 10, 1960 because of vomiting for two weeks. She was well, except for "indigestion" relieved by bicarbonate for at least twenty years and occasional spicy food tolerance, until July 1960 when she experienced a one week episode of vomiting following meals. There was some associated epigastric bloating and substernal chest pain. At the end of the one week period her difficulties spontaneously disappeared. Fifteen days prior to admission she again developed the same symptoms. However, this time the vomiting persisted. She had no melena, jaundice or acholic stools. The vomiting occurred almost immediately after food ingestion. Again she noted postprandial epigastric bloating and non-radiating pain in the epigastrium. Although the patient was able to pass gas per rectum at the time of admission, she had not had a bowel movement for six days. Her past medical history, family history and review of systems were non-contributory.

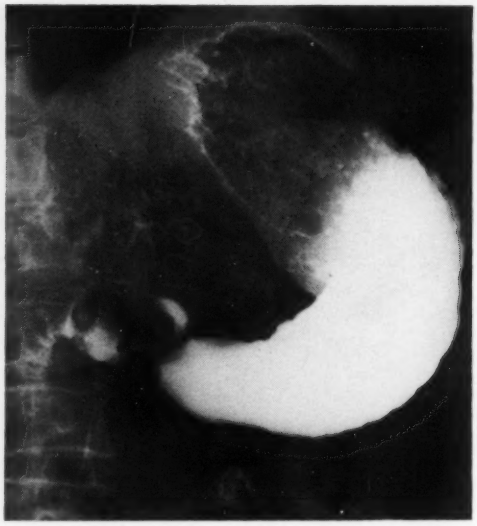
On admission she was not complaining of pain. Physical examination revealed marked distension of the abdomen, mostly in the left upper quadrant and in the mid epigastrium. The remainder of the examination was not remarkable.

Her hemoglobin was 12.1 gm.; her white cell count and differential count were within normal limits. A non-catherized urine specimen revealed 10-15 white cells per high power field. Plasma chlorides were 94 meq./liter, plasma CO_2 was 25 meq./liter, plasma sodium was 137 meq./liter and plasma potassium was 3.2 meq./liter.

A Levin tube was inserted into the stomach and approximately 2700 cc. of bile stained gastric contents were removed. There was a marked deflation of the abdomen with this procedure. Roentgen examination of the upper gastrointestinal tract revealed a 4 cm. oval defect in the duodenal bulb with dilation of the stomach

Dr. Rosenbaum is a resident, Department of Radiology; Dr. Glassman is an assistant, Department of Surgery and Dr. Alden is Attending Chief, Department of Radiology, Delaware Hospital, Wilmington.





and only minimal passage of barium into the duodenal loop. There was a collection of barium within the gallbladder and the biliary ducts. An operative procedure was done on the third day after admission. On exploration there was a large inflammatory mass in the right upper quadrant involving the porta hepatis and first portion of the duodenum. The gallbladder was densely adherent to the first portion of the duodenum where a large communication existed between the two organs. In the duodenum a black, firm stone measuring approximately 5 cm. in greatest dimensions was found. The duodenum, gallbladder and porta hepatis were diffusely involved in a chronic indurative process which rendered almost all of the structures undefinable. The common duct was dilated and no stones were present in the lumen. A soft rubber catheter could easily be passed through the common duct into the duodenum.

The patient's post-operative course was completely uneventful and she was discharged on her tenth post-operative day. She was eating well and had no pain for the first time in twenty years. She was seen at one month and two months after her surgery and was asymptomatic.

REFERENCES

1. Berens, David L.: Gallstones impacted in duodenal bulb. Gastroenterology 36: 881-883, 1959.
2. Borman, C. N., and Rigler, L. G.: Spontaneous internal biliary fistula and gallstone obstruction, with particular reference to roentgenologic diagnosis. Surgery 1: 349-378, 1937.
3. DeFoe, E., and Meigher, S. D.: Gallstones impacted in the stomach and duodenal bulb demonstrated by roentgenologic examination. Am. J. Roentgenol. 77: 40-46, 1957.

REPRINTS AVAILABLE

Reprints of the four Combined Clinical Staff Conferences of the N.I.H., published in the Annals of Internal Medicine, are now available upon request and are as follows: "Unexplained Death in a Patient with Leukemia;" "Recurrent Pulmonary Disease in a Child;" "Problem in Differential Diagnosis;" and Primary Amyloidosis."

DIAGNOSIS OF NEOPLASTIC TISSUE OF THE BRAIN AND OTHER ORGANS

With Rio Hortega's Rapid Ammoniated Silver Carbonate Impregnation†

• The authors desire to introduce Rio Hortega's rapid ammoniated silver carbonate impregnation method with their variants for the diagnosis of all neoplastic tissues regardless of their origin. They are fully convinced by their own success that this is not just another method which will burden the pathologist but one on which he can thoroughly depend.

J. R. Ravens, M.D.
L. L. Adamkiewicz, M.D.
R. A. Groff, M.D.
P. D. Gordy, M.D.

The clinician and the neuro-surgeon always hoped to be able to diagnose the ailments of their patients quickly and institute the indicated treatment without delay. These objectives made it necessary for other diagnosticians, the pathologist for one, to invent new rapid means of staining which could be compared with the routine methods in presenting a true and constant picture on which the diagnosis could be made.

Many rapid methods are available to the pathologist but all fail him in some way. When Rio Hortega, 1919,[24] developed his rapid ammoniated silver carbonate method, he provided what appears to be the most convenient dependable method which in experienced hands will offer an almost ideal approach to the desired diagnosis and a method which is quite comparable to the tested routine procedures as regards fidelity of reproduction, dependability and ease of performance. The few illustrations which accompany this study are the best assurance of the merits of this technique.

Material

For three years the authors submitted surgically removed tissues including nervous tissues to this method as these were delivered to the laboratory for rapid diagnosis. The gratifying results obtained greatly increased their interest in this simple and economical method. They consider it worthy of more general usage more particularly since it requires only five to six minutes for its performance.

During the time of its usage the authors added two variants to the general rapid method devised by Rio Hortega. These variants require only a few additional moments and augment and facilitate the microscopic interpretation.

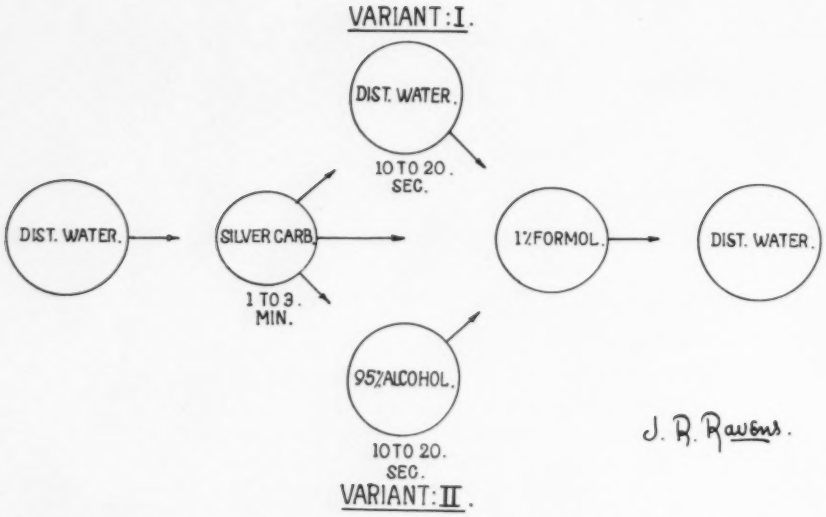
Dr. Ravens is Neuropathologist, Graduate Hospital, University of Pennsylvania; assistant in Neuroanatomy and Neuropathology, at its Graduate School of Medicine.

Dr. Adamkiewicz is Pathologist, Doctor's Hospital, Philadelphia.

Dr. Groff is Professor of Neurosurgery, Medical School and Graduate School, Univ. of Penn.; Chief Departments of Neurosurgery, University and Graduate Hospitals, Univ. of Penn.

Dr. Gordy is Chief, Departments of Neurosurgery, Delaware Hospital, Wilmington.

†From the Departments of Neuropathology and Neurosurgery of the Graduate Hospital of the University of Pennsylvania, and the Departments of Surgical Pathology and Neurosurgery of the Delaware Hospital, Inc.



Schematic diagram showing manner or the procedure of the rapid silver impregnation and position of the different staining dishes.

THE VALUE OF THE METHOD AND ITS TWO VARIANTS

To obtain silver impregnation it is necessary to provide the following:

A. Materials Required

1. Dishes
   a) 36mm in diameter, 10 cc capacity, for the silver solution.
   b) 50mm in diameter, 30 cc capacity, for alcohol, distilled water and one percent formol solution.
   c) 60mm in diameter, 50 cc capacity, for distilled water as illustrated in the schematic diagram.
2. A thin glass rod (3mm in diameter) tapered at right angles for handling sections.
3. Amber glass stoppered bottles for silver and all other solutions employed.
4. Dropping bottles.
5. Slides and cover glasses of various sizes.
6. Filter paper in sheets cut to convenient size for blotting sections.

B. Solutions Required

1. *10 per cent Formaldehyde solution*

40% commercial formaldehyde	1 part
Tap water	4 parts

For use in fixation of blocks of tissues. These proportions express the concentration of formaldehyde solution in terms of the formalin content. The small error due to the fact that formalin is not exactly 40% formaldehyde may be disregarded for most purposes.

2. *Neutral formaldehyde solution*

40% commercial formaldehyde	1000 cc
Calcium carbonate	15 gms.

If calcium carbonate is not available magnesium carbonate may be used in the same amount. The best way to ensure the neutrality of formaldehyde and its dilutions is to employ an indicator such as phenolphthalein in alcohol and add sufficient amount of 10% sodium hydroxide to bring out a faintly pink color.

3. *1 per cent neutral formaldehyde solution*

Neutral 40% commercial formaldehyde

	1 cc
Distilled water	100 cc

4. *1/500 gold chloride solution*

Gold chloride	1 gm.
Distilled water	500 cc

5. *5 per cent sodium thiosulfate solution*

Sodium thiosulfate	5 gms.
Distilled water	100 cc

6. *10 per cent silver nitrate solution*

Silver nitrate	10 gms.
Distilled water	100 cc

7. *5 per cent anhydrous sodium carbonate solution*

Anhydrous sodium carbonate	5 gms.
Distilled water	100 cc

This solution should be freshly prepared.

8. *Medium strength ammoniated silver carbonate solution*

10% silver nitrate	5 cc
5% Anhydrous sodium carbonate	15 cc

Concentrated ammonium hydroxide (*drop by drop*) *until the precipitate is completely dissolved*

Distilled water	20 cc

Of the three concentrations of ammoniated silver carbonate devised by Rio Hortega[32] — weak, medium, and strong — the medium strength definitely fulfills the requirements best as regards the delineation

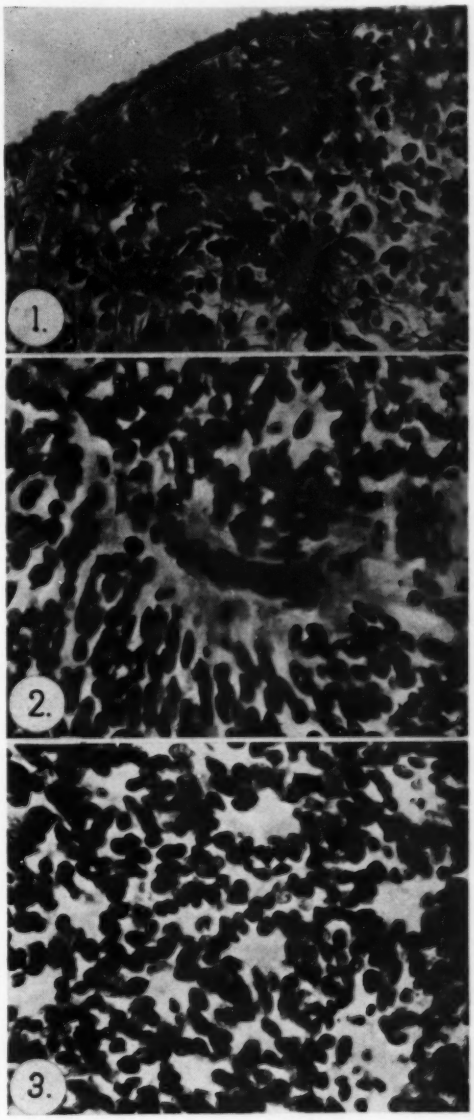


Fig. 1. Ependymoma (Glioepithelioma, Rio Hortega's Classification), showing a diffuse distribution of the tumor cells with large rounded or oval nuclei. Note that in the upper part of the illustration represent glioependymal cells lining the surface of the tumor; Ammoniated silver carbonate-formol (Rio Hortega's general impregnation).

Fig. 2. Ependymoblastoma (Glioblastoma isomorpho, Rio Hortega's Classification). Fairly marked orientation of tumor cells to blood vessels. Note characteristic shape of nuclei and tendency of tumor cells to form "gliovascular system;" Ammoniated silver carbonate - water - formol (Variant I).

Fig. . Medulloblastoma (Neuroblastoma, Rio Hortega's Classification). The tumor cells are arranged in pseudorosette formation; Ammoniated silver carbonate - alcohol - formol (Variant 11).

of the architecture of the tissue and ensures the proper intensity of staining. It was found that with the weak solution the depth of impregnation was spotty and irregular while with the strong solution the depth of staining was increased so much that contrast was not properly developed. The solution is ready for use in 4 to 8 days and improves with age.

C. Clearing Mixtures

1. *Carbolic acid - Xylol*

Carbolic acid	20 cc
Xylol	60 cc

or

2. *Carbolic acid - Creosote - Xylol or Toluol*

Carbolic acid	10 cc
Creosote	10 cc
Xylol or Toluol	80 cc

Carbolic acid crystals are dissolved by heating. This solution should be freshly prepared to facilitate clearing and handling of the tissues.

Note: All solutions employed are kept in amber colored bottles.

Method

1. *Fixation of the tissue is accomplished in 10 per cent boiling formaldehyde solution*

Tissue blocks of appropriate size and 3 to 4 mm in thickness, are placed in boiling formaldehyde for 1 to 2 minutes. When time is not pressing the boiling may be slightly prolonged. Adequate fixation is essential for proper impregnation of the sections. Formaldehyde is the best fixative for any metallic impregnation and the specified thickness of the tissue is optimum.

2. *Washing the tissue in running tap water*

Washing is necessary for the prompt elimination of an excess of formaldehyde.

3. *Cutting of frozen sections*

These are cut at a thickness of 10 to 15 micron and are placed in distilled water or if desired directly into the ammoniated silver carbonate solution which is greatly warmed beforehand (45 to 50°C in oven).

4. *Impregnation of sections in silver carbonate solution*

Sections are transferred to medium strength silver carbonate solution for 1 to 3 minutes. During this interval the section should show no coloration or should turn a yellowish-gray.

5. *Reduction of impregnated sections in 1% neutral formaldehyde solution*

Sections are then immersed and gently agitated in the latter solution until they display a brownish-yellow color. If the sections turn yellow-gray in this step, it indicates that the period of impregnation in step 4 was too short and this requires a repetition of steps 4 and 5. In this reducing procedure the formaldehyde solution turns blackish-gray.

6. *Washing sections in distilled water*

The sections are placed in distilled water to eliminate the excess of the reducing agent. The sections are now floated onto slides and examined while still wet or are processed by dehydration for permanent mounting, since now the maximum of nuclear impregnation and differentiation of the cell cytoplasm and of the supporting stroma have occurred for microscopic examination.

Although the impregnation is completed at this point, further accentuation of the architecture of the parenchyma and stroma may be achieved in the following manner:

7. *Toning of sections in 1/500 gold chloride solution*

Sections are placed in the latter solution for 30 seconds at room temperature or until they take on a uniformly gray color. This step is optional. It reduces over impregnation with silver giving a lighter stroma and greater contrast.

8. *Fixing of sections in 5% sodium thiosulphate*

The sections are placed in the mentioned solution of 10 to 20 seconds.

9. *Washing sections in distilled water*

The excess of sodium thiosulphate is removed by washing, and the preparations are ready for permanent mounting.

10. *Dehydration, clearing and mounting*

Only two alcohols are employed in this process, 80% and 95%. The use of absolute alcohol is not recommended as it produces

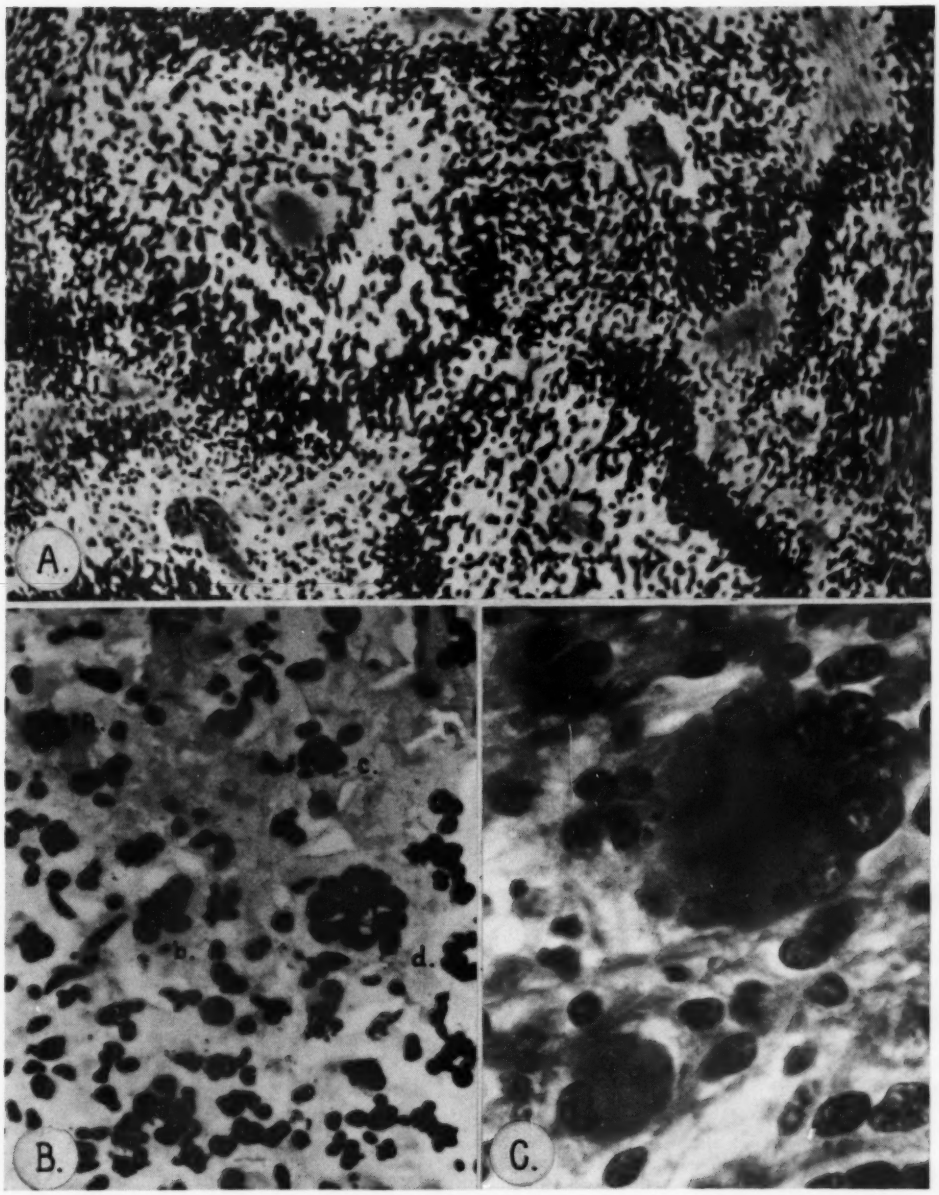


Fig. 4. Glioblastoma multiforme (Glioblastoma heteromorpho, Rio Hortega's Classification). Three different aspects of the tumor: A, showing small areas of initial necrosis and tumor cells grouping about necrotic areas in palisade formation. Note marked cellular polymorphism; B, marked cellular polymorphism of the tumor cells diffusely scattered throughout the stroma. Note isolated giant tumor cells with many nuclei (a, b, c, and d); Ammoniated silver carbonate-formol (Rio Hortega's general impregnation); and C, two giant tumor cells showing typical cytomorphologic characteristics; Ammoniated silver carbonate - water - formol, (Variant I).

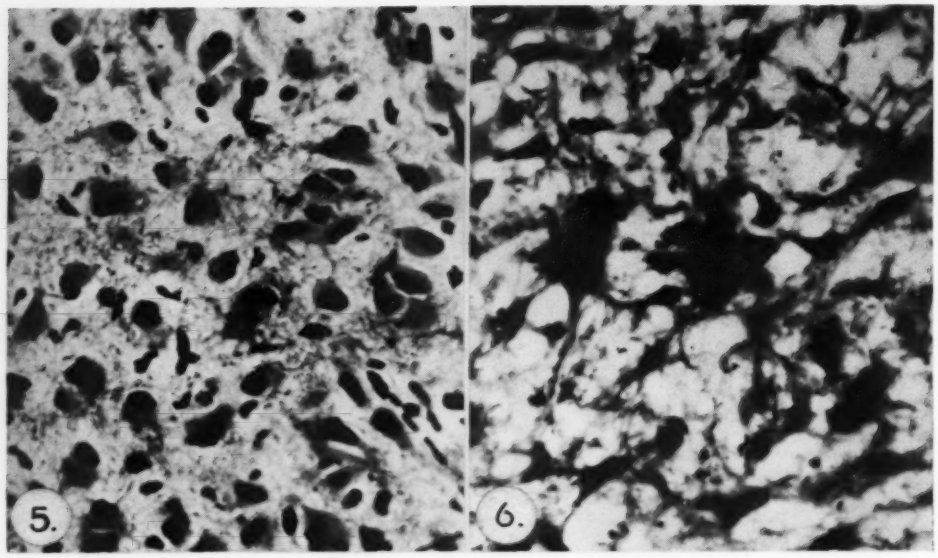


Fig. 5. Protoplasmic astrocytoma (Protoplasmic astrocytoma, Rio Hortega's Classification). Diffuse distribution of tumor cells having abundant angular cytoplasmic extensions and eccentric large oval or rounded nuclei; Ammoniated silver carbonate - alcohol - formol (Variant II).

Fig. 6. Fibrillary astrocytoma (Fibrillary astrocytoma, Rio Hortega's Classification). Two giant astrocytic tumor cells surrounding smaller similar cells; Ammoniated silver carbonate - alcohol - formol (Variant II).

shrinkage of the tissue. Carbol-xylol or carbol-creosote-toluol mixtures are considered best for clearing the sections. Blotting with dry filter paper without pressure and mounting in balsam completes the procedure.

Thus with rapid ammoniated silver carbonate impregnation, two types of microscopic preparations are possible; a *rapid temporary* and a *permanent* preparation.

The addition of the two following variants performed simultaneously with the general procedure greatly facilitates the study of nuclear and cytoplasmic definition of the neoplastic cells and their supporting stroma.

Variant I. Ammoniated Silver Carbonate - Water - Formaldehyde

1. Frozen sections are placed in distilled water.
2. Medium ammoniated silver carbonate solution for 1 to 3 minutes.
3. *Wash sections individually in distilled water for 10 to 20 seconds.*
4. Reduce in 1% neutral formol solution.
5. Wash in distilled water.

The sections are now placed on the slide and are ready for examination either wet or they may be processed as permanent sections (see above). The introduction of step 3 in the general technique permits better visualization of the nuclear structure of the neoplastic cell as well as the supporting connective tissue, blood vessels and of inflammatory and wandering cells.

Variant II. Ammoniated Silver Carbonate - Alcohol - Formaldehyde

1. Frozen sections are placed in distilled water.
2. Medium ammoniated silver carbonate solution for 1 to 3 minutes.
3. *Wash sections individually in 95% or*

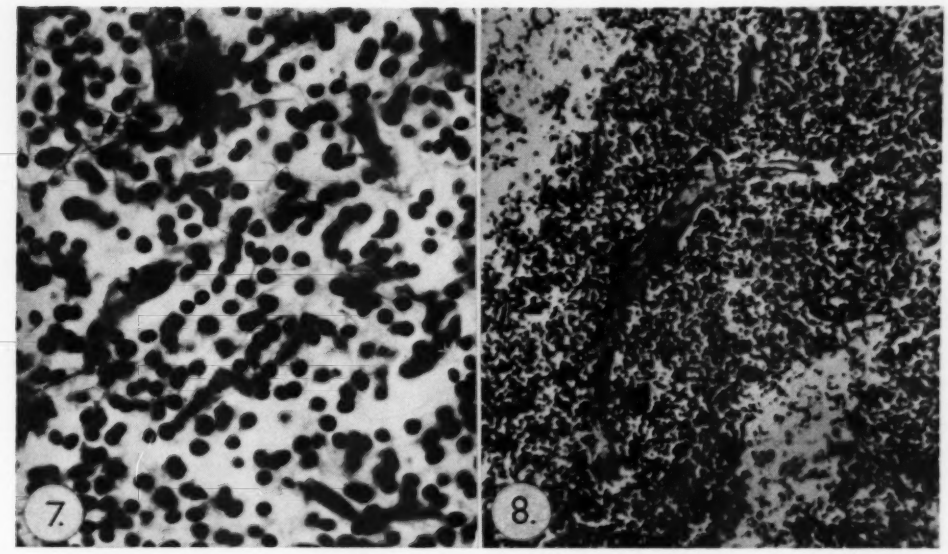


Fig. 7. Oligodendroglioma (Oligodendroglioma, diffuse type, Rio Hortega's Classification). Marked diffuse distribution of the neoplastic cells throughout the tumor. Note the small blood vessels are intermingled with the tumor cells; Ammoniated silver carbonate - formol (Rio Hortega's general impregnation).

Fig. 8. Neuroblastoma (Neuroblastoma, Rio Hortega's Classification). Mass of tumor cells grouped around a blood vessel; Ammoniated silver carbonate - formol (Rio Hortegas general impregnation).

absolute alcohol for 10 to 20 seconds.

4. Reduce sections in 1% neutral formol solution.
5. Wash in distilled water.

The sections are now placed on the slide, and are ready for examination either wet or they may be processed as permanent sections (see above). The introduction of step 3 in the technique permits better study of the cytoplasm of the neoplastic cells as well as of the supporting stroma.

These steps are clearly illustrated in the schematic drawing.

Results

The study of the various tissues of the body convinced the authors of the reliability and value of this rapid method of staining.

The simultaneous employment of the ammoniated silver carbonate general technique with its two variants facilitates the study of the architecture of the parenchyma and stroma of the neoplasm thus simplifying the diagnosis, which may be made in a surprisingly short time.

With the above method the nuclei of the tumor cells are stained black or brownish-violet while the mitotic figures stain deep black. The cytoplasm of these cells is yellow or yellowish-brown and the connective tissue fibers, principally the collagenous ones are red violet or a yellowish-brown. It is interesting that with this method the connective tissue cells encountered in the supporting stroma will exhibit many surprisingly clear and unexpected details of their structure. These cells will appear as elongated, angulated or branching, showing vacoules or granular inclusions in the cytoplasm while the structure of the blood vessel is vivid and precise. Inflamatory cells present in the connective tissue

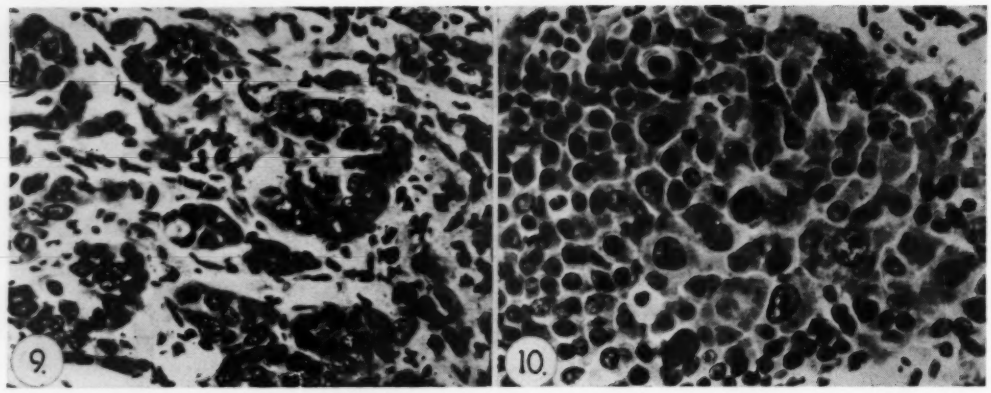


Fig. 9. Infiltrating duct carcinoma of breast. Tumor cells extending in interlacing cords and nests in dense connective tissue; Ammoniated silver carbonate - formol (Rio Hortega's general impregnation).

Fig. 10. Infiltrating transitional cell carcinoma of the urinary bladder. Mass of undifferent tumor cell with marked cellular polymorphism. Note the large rounded nuclei with prominent nucleoli and scanty cytoplasm; Ammoniated silver carbonate - formol (Rio Hortega's general impregnation).

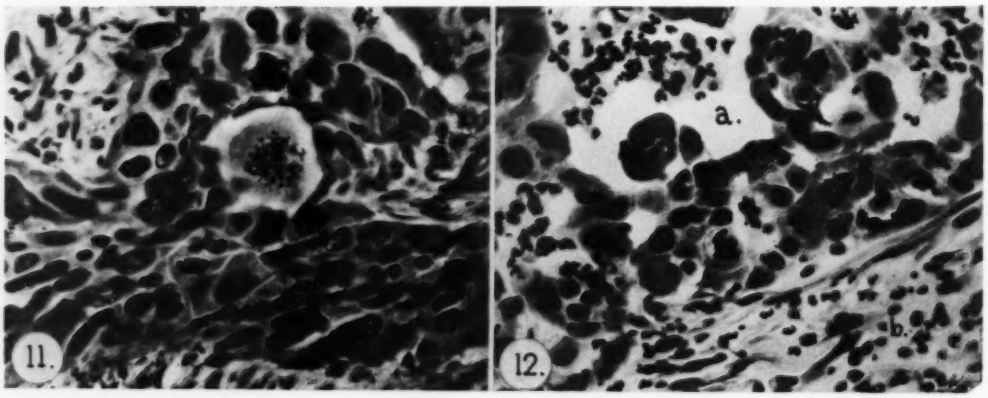


Fig. 11. Bronchogenic carcinoma, squamous cell type. A group of tumor cells extending in cords varying in size and shape; Ammoniated silver carbonate - water - formol (Variant I).

Fig. 12. Comedocarcinoma of the breast. Segment of duct showing arrangement of the neoplastic cells. Note in (a) partially filled lumen with inflamatory cells, and (b) elongated fibroblasts and fibers loosely surrounding the periphery of the duct; Ammoniated silver carbonate - alcohol (Variant II).

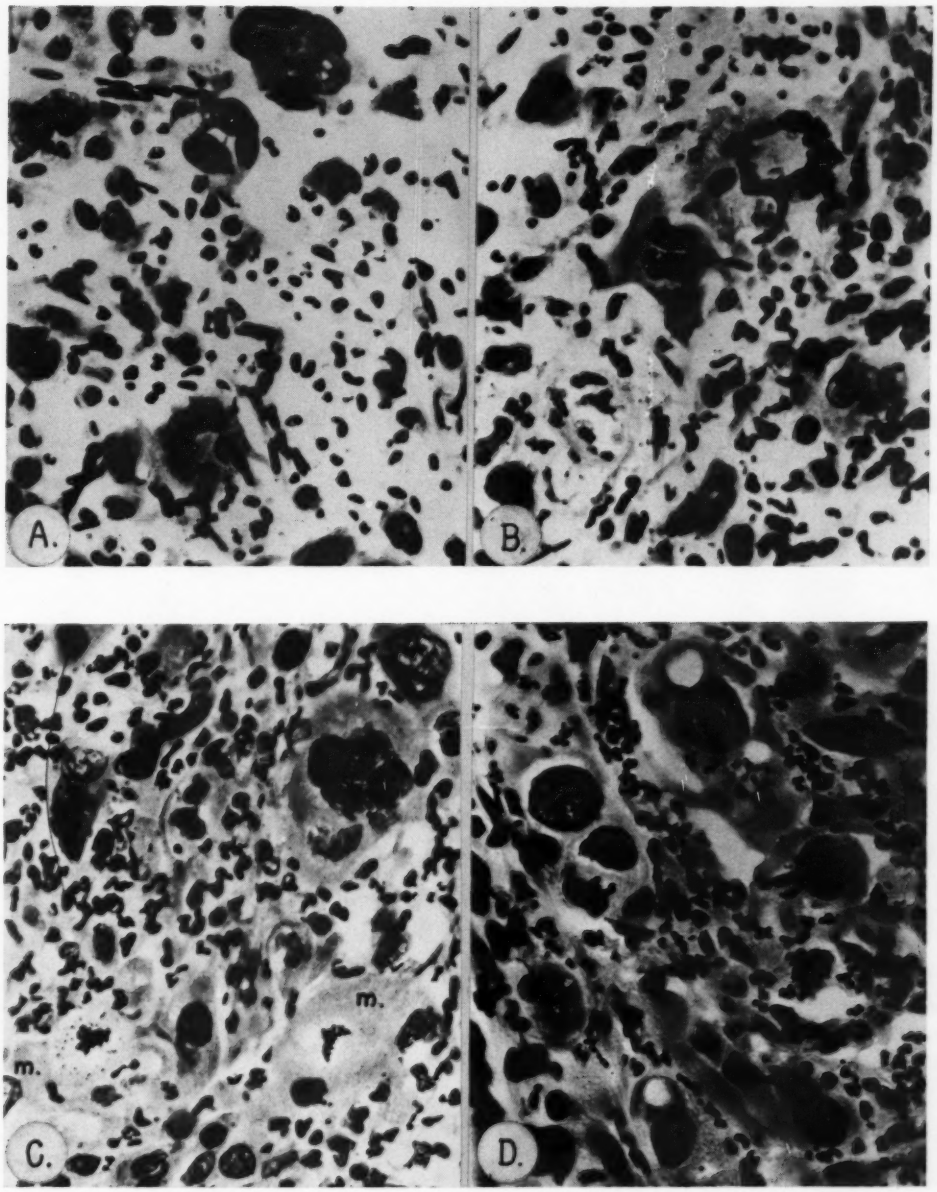


Fig. 13. Neoplastic cells: A and B, Anaplastic cells in bronchogenic carcinoma showing various sizes and shapes in the cellular morphology; Ammoniated silver carbonate - formol (Rio Hortega's general impregnation). C, Anaplastic tumor cells from carcinoma of the breast and atypical mitotic figures (m); Ammoniated silver carbonate - -water - formol - (Variant I); and D, Anaplastic tumor cells in carcinoma of the stomach showing large rounded nuclei with prominent nucleoli scanty cytoplasm. Note the presence of vacuoles in the cytoplasm of two tumor cells; Ammoniated silver carbonate - alcohol -formol (Variant II).

such as histiocytes, monocytes, lymphocytes, plasma cells and polymorphonuclear leukocytes are also clearly visualized.

From the illustrations accompanying this study, it is clear that the ammoniated silver carbonate impregnation may permit rapid diagnosis. It is also evident from the excellent impregnation of different structures that this technique is of value not only in practical application but also in its basic or academic aspects.

The diagnosis of ependymomas, ependymoblastomas and medulloblastomas shown in figures 1, 2 and 3 respectively is relatively easy because of the characteristic distribution and disposition of the tumor cells. Thus, figure 1 shows differentiated ependymal cells with a grouping in masses and a tendency to form "*true rosettes.*" In figure 2 the less differentiated ependymal cells are characteristically disposed around the blood vessels with a tendency to form "*gliovascular systems*" of Rio Hortega,, while figure 3 shows a distinct formation of "*pseudorosettes*" which are fairly characteristic of the medulloblastoma.

The more interesting findings developed in this manner occur in the glioblastoma multiforme in which the rich vascularity of the tumor, its cellular polymorphism and its tendency to palisade formation are demonstrated. Figure 4 A, B and C shows aspects of the architecture of this tumor.

By this method the nature of astroblastomas and astrocytomas is clearly revealed by demonstrating the cytoplasmic processes of their cells. Figures 5 and 6 clearly illustrate the protoplasmic and fibrillary types of astrocytoma.

Very cellular tumors such as oligodendrogliomas and neuroblastomas may be confusing and difficult to diagnose, but one may perceive some difference between these tumors. In the oligodendrogliomas abundant small blood vessels are intermingled with the tumor cells, while in the neuroblastomas the tumor cells, have a tendency to surround a small blood vessel and to form pseudorosettes. These characteristics are illustrated in figures 7 and 8. The application of this method in the diagnosis of other tumors brings out their details with remarkable clarity as can be seen in figures 9, 10, 11 and 12. In figure 13, A, B, C and D different types of highly anaplastic cells in various tumors are illustrated. Their cells are so well defined structurally and morphologically that confusion cannot occur.

Finally, typical and atypical mitotic figures are beautifully brought out by the metallic impregnation as can be observed in figures 13C, and 14.

Discussion

The development of microscopic anatomy has contributed much to knowledge concerning health or disease of tissues. Many of the significant discoveries in the field of medicine were revealed with the aid of metallic impregnation. Even the use of the proposed simple silver impregnation technique in this paper reveals much as indicated in the accompanying illustrations. With this method the pathologist can be assured of an easier interpretation of the microscopic picture, because the architecture is so well revealed and is less adequately brought out by other methods. In a review of the literature, the authors failed to find an impregnation method applied to general body tissue.

In 1918, Rio Hortega[23] observed that his practical method of ammoniated silver carbonate could be applied to general body tissue as well as to nervous tissue. While he and his followers gained fame with their silver impregnation methods and gave us much of the knowledge of nervous tissues we have today, the application of this method to general body tissues was all but forgotten. The latter, however, in the hands of Rio Hortega, because of its simplicity, directness and gratifying results also did much to further our information in general histology of tissues. The structures developed by this method are so clearly defined that it can be compared with the impregnation methods of Cajal,[7,8] Bielschowsky,[4] and Achucarro.[1,2]

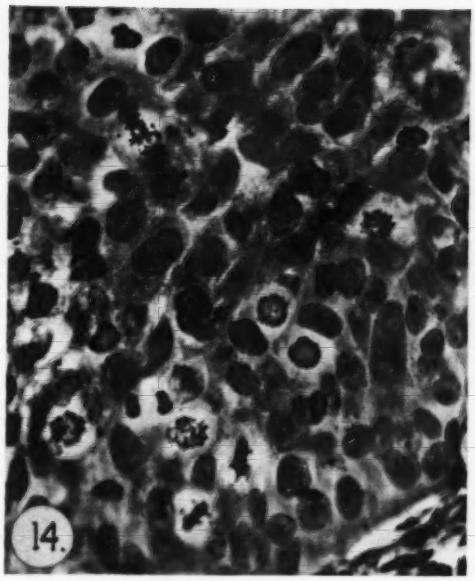


Fig. 14. Squamous cell carcinoma of the larynx, showing the characteristic arrangement of the neoplastic cells and numerous typical and atypical mitotic figures; Ammoniated silver carbonate - water - formol (Varient I).

In 1936, Sanchez-Perez[37] described Rio Hortega's silver impregnation with different variants and their practical uses in histologic studies. Similarly, German[12] in 1938 published three paper dealing with many of Hortega's silver impregnation.

This information was gratefully received in general but relatively few adopted its employment although the interest in it continues to increase to date.

Among the outstanding investigators in the latter group who made many contributions in the literature supporting the universal applicability of the ammoniated silver carbonate impregnation method are. Alberca Lorente, Alvarez Cascos, Bruno, Collado, Costero, Encinas, Gallego, Jabonero, Jimenez De Asua, Lopez Enriquez, Ortiz Picon, Perez Lista, Polak, Prado and many others. In the United States and Canada such investigators as Alpers, Bailey, Bucy, Cone, Courville, Ferraro, Globus, Haymaker, Kernohan, Penfield, Scharenberg, Weil and others also made excellent contributions by this method.

In 1948, Yue, Riley, Miller and Scharenberg[42] applied this method of staining to vaginal and cervical smears with satisfactory results. While later, in 1950 Cabieses-Molina[6] in collaboration with Adamkiewicz applied the rapid ammoniated silver carbonate method to "smears" from brain tumors. They found this method interesting and useful in the study of the cytology of the tumors arising in nervous tissue. These authors found that the components of the architecture of the gliomas are well brought out by this method. However these innovations are not new since Rio Hortega in Spain, Moyano, Prado and Polak in Argentina, Bruno in Uruguay, Encinas, Ravens and Olga Palacios in Peru, Ortiz Picon in Colombia, Herrera in Panama, Leon Blanco in Cuba, Costero in Mexico and many others had used this method extensively with excellent results. This method is admittedly very useful and interesting when applied to the study of the morphology of the individual tumor cell but in order to obtain a bird's eye view of the whole picture, better results will follow when ammoniated silver carbonate impregnation is applied to frozen sections.

Conclusion

In the present paper the authors present Rio Hortega's rapid ammoniated silver carbonate impregnation method and also introduce two variants for a better differentiation of the neoplastic tissue in the brain and other organs.

The ammoniated silver carbonate impregnation is easily carried out. It permits a splendid contrast in the resulting pictures with little effort and expense.

ACKNOWLEDGEMENTS

The authors want to express their thanks to the Doctors A. Valdez-Dapena and John W. Howard, the directors of the laboratories of the Graduate Hospital of the University of Pennsylvania and the Delaware Hospital, Inc. respectively, for their kindness in making this study possible. Our appreciation is also expressed to Mrs. Lucille Ravens, who has been of great assistance in the final preparation of the manuscript.

REFERENCES:

1. Achucarro, N.: Nuevo método para el estudio de la neuroglía y del tejido conjuntivo. Bol. de la Soc. Esp. de Biol. Vol. 1:12, 1911.
2. Algunos resultados histopatológicos obtenidos con el procedimiento del tanino y la plata amoniacal. Trab. de Lab. de Inv. Biol. de la Univ. de Madrid. Vol. 9: 269-288, 1911.
3. Baker, J. R.: Cytological Technique, p.p. 45-54, 3rd. Edition, John Wiley & Sons, Inc. New York, 1950.
4. Bielschowsky, M.: Die Silberimprägnation der Neurofibrillen. Journ. f. Psychol. u.Neurol. Vol. 3: 169-189, 1904.
5. Bullo, J.: Contribución de la Escuela de Cajal sobre Histopatología de la Neuroglia y Microglia. Arch. de Hist. normal y patol. Vol. 2: 425-445, 1943-45.
6. Cabieses - Molina, F.: Una técnica rápida para el estudio de biopsias cerebrales. Rev. Neuro-psiquiat. Vol. 13: 651-656, 1950.
7. Cajal, S. Ramon y.: Sobre un nuevo proceder de impregnación de la neuroglia y sus resultados en los centros nerviosos del hombre y los animales. Trab. del Lab. de Inv. Biol. de la Univ. de Madrid. Vol. 11: 279-237, 1913.
8. and De Castro, F.: Elementos de Técnica Midrográfica del Sistema Nervioso. Tipografía Artística. Madrid, 1933.
9. De Castro, F.: Pio del Rio Hortega.—Trab. del Inst. Cajal de Invest. Biol. Vol: 37: 7-18, 1945.
10. Encinas, E.: Don Pío del Río Hortega.—Bosquejo parcial de su obra.—Rev. de Neuro, psiq. Vol. 8: 262-387, 1945.
11. Fajersztajn, J.: Ein neues Silberimpragnationsverfahren als Mittel zur Farbung der Axencylinder. Neurol. Centralbtt. Vol. 20: 98-106, 1901.
12. German, Wm. M.: Hortega's Silver impregnation technique uses and application. Amer. J. of Clinic Pathol., Technical Supplement. Vol. 8: 165-171, 1938; Vol. 9: 13-19 and 47-55, 1939.
13. Globus, J. H.: The Cajal and Hortega glia staining methods. A new step in the preparation of formaldehyde—fixed material. Arch. Neurol. and Psichiat. Vol. 18: 263-271, 1927.
14. Kubie, L. S. and Davidson, D.: The Ammoniacal Silver Solution used in Neuro-pathology. Arch. Neurol. and Psyciat. Vol. 19: 888-903, 1928.
15. Moyano, B. A.: La obra científica de Don Pío del Río Hortega. Publicación del Laboratorio de Anatomía Patológica del Hospicio de las Mercedes. Buenos Aires, 1946.
16. Penfield, W. G.: A method of staining oligodendroglia and microglia (combined method). Am. Journ. of Pathol. Vol. 4: 153-157, 1928.
17. Polak, M.: Pío del Río Hortega. Arch. de Hist. normal y patol. Vol. 3: 377-421, 1947.
18. Prado, J. M.: Las Técnicas en el estudio histopatológico del sistema nervioso., Tesis. Buenos Aires, 1939.
19. Ravens, J. R.: Employment of Copper Sulphate and Sodium Perborate Ammoniated Silver Nitrate Impregnation Method in Central and Peripheral Nervous System (To be published
20. Ammoniated Silver Nitrate and its variants, a new impregnation method for study of nervous as well as other tissues. (To be published).
21. A new metallic impregnation for the development of the architectural components of the cerebellum. (To be published).
22. Rio Hortega, P. del.: Noticia de un nuevo y fácil método para la coloración de la neuroglía y del tejido conectivo. Trab. del Lab. de Inv. Biol. de la Univ. de Madrid. Vol. 15: 367-378, 1917.
23. Un nuevo método de investigación histológica e histopatológica. Bol. de la Soc. Espan. de Biol., 1918.
24. Coloración rápida de tejidos normales y patológicos con Carbonato de Plata Amoniacal. Trab. del Lab. de Inv. Biol. de la Univ. de Madrid. Vol. 17: 229-235, 1919.
25. La microglía y su transformación en células en bastoncito y cuerpos granulos adiposos. Trab. del Lab. de Inv. Biol. de la Univ. de Madrid. Vol. 18: 37-82, 1920-21.
26. Una sencilla técnica para teñir rápidamente neurofibrillas y fibras nerviosas. Bol. de la Soc. Espan. de Hist. Nat. Vol. 21: 364-371, 1921.
27. Coloración selectiva de pigmentos y prepigmentos. Bol. de la Soc. Espan. de Hist. Nat. Vol. 25: 122-126, 1925.
28. Varias técnicas selectivas para tinción del tejido conectivo reticular. Bol. de la Soc. Espan. de Hist. Nat. Vol. 25: 204-210, 1925.
29. Manera sencilla de tenir, epiteliofibrillas y ciertos reticulos protoplásmicos de defícil demonstración. Bol. de la Soc. Espan. de Hist. Nat. Vol. 26: 107-113, 1926.
30. Innovaciones útiles en la técnica de coloración de la microglía y otros elementos del sistema macrófago. Bol. de la soc. Espan. de Hist. Nat. Vol. 27: 199-210, 1927.
31. Arte y artificio de la ciencia histológica. Residencia, Revista de la Residencia de Estudiantes, Madrid. Vol. 4: 191-206, 1933.
32. Rio Hortega, P. del.: El método del Carbonato Argéntico, Revisión General de sus Técnicas y Aplicaciones en Histologia Normal y Patológica. Arch. de Hist. normal y patol. Vol. 1: 165-205, 1942; Vol. 2: 231-244 and 577-604, 1943.
33. Robertson, W. F.: On a new metod of obtaining a black reaction in certain tissue elements of central nervous system (platinum method). Scot. med. and Surg. J. Vol. 4: 23, 1899.
34. Platinum Method for Central Nervous System. Jour. Ment. Sci. Vol. 46: 352, 1900.
35. Samuel, E. P.: Impregnation and Development in Silver Staining. J. Anat. Vol. 87: 268-277, 1953.
36. The Mechanism of Silver staining. J. Anat. Vol. 87: 278-287, 1953.
37. Sanchez, Perez, J. M.: Hortega's Silver Stains in Neuropathology. J. Techn. Meth. and Bul. Intlernat. Ass. Med. Bus. Vol. 15: 74-83, 1936.
38. Scharenberg, K.: Pio del Río Hortega. (1882-1945). In the Founders of Neurology, p.p. 86-89, Charles C. Thomas, Springfield, Illinois, 1953.
39. Simarro, L.: Nuevo método histológico de impregnación por las sales fotográficas de Plata. Rev. Ibero Am. de Cien. med. Vol. 4: 332-358, 1900.
40. Simarro, L.: Nuevo método histológico de impregnación por las sales fotográficas de plata. Rev. Trim. Micr. Vol. 5: 45, 1900.
41. Tello, J. F.: Cajal y su labor histológica, p.p. 103-109. Tipografía Artística, Madrid, 1935.
42. Yue, H. S.; Riley, G. M.; Miller, N. F. and Scharenberg, K.: The application of a silver carbonate stain for the diagnosis of uterine cancer by the vaginal smear method. Am. J. Obst. and Gynec. Vol. 56: 468-478, 1948.

IN MEMORIAM

The death at age 61 of Louis M. Orr, M.D., immediate past president of the A.M.A., is a loss to the medical profession. Dr. Orr was a distinguished urologist and surgeon who carried on a fearless campaign to preserve the private practice of medicine in this country. Dr. Orr will be remembered for his appearance at the Delaware Academy of Medicine in October, 1959, when he participated in the "Seminar on Aging" at the Annual Meeting of the Medical Society of Delaware.

President's Page

Samuel C. McCue

CONFIDENTIALITY OF MEDICAL RECORDS

Section 9 of the Principles of Medical Ethics of the American Medical Association enunciates the standard of conduct with respect to confidences entrusted by patients to a physician as follows:

> "A physician may not reveal the confidences entrusted to him in the course of medical attendance, or the deficiencies he may observe in the character of patients, unless he is required to do so by law or unless it becomes necessary in order to protect the welfare of the individual or of the community."

The public welfare and safety, the well-being of people as a whole, takes precedence over individual privilege. Thus, there are legal requirements to report instances of communicable disease to designated health authorities as an essential step in controlling the spread of such disease. Birth certificates provide evidence as to age, citizenship, family relationships and related needs both of the individual and of the society in which he lives. Death certificates supply information of utmost importance to bereaved families, and to various medical health and welfare organizations. There are laws requiring physicians to report injuries actually or possibly inflicted with firearms, knives and other weapons.

Beyond the requirements of law, there are other inroads on the confidentiality of medical records. The burgeoning in recent years of health insurance plans, sickness and disability payments by employers, retirement programs and similar intrusions of valid third party interests have complicated the patient-physician relationship. A physician can protect his position in the eyes of the patient 1) by obtaining the patient's consent to release information contained in the medical record, and 2) by supplying only the information which is actually pertinent to the needs of the situation. Under legal requirements the physician should know the purpose of the law so that discretion may be used in determining the amount and type of information to be supplied. To satisfy claims under health insurance and other benefit plans the physician should select and disclose only those facts which expedite the adjudication of the claims and the payment of proper benefits.

Ethically the physician should assure himself that the patient, his relatives, his responsible friends or agents or legitimate third party concern have such knowledge of the patient's condition as will serve the best interests of the patient. Fortunately, in most instances this does not require violating confidences or revealing deficiencies the physician may observe in the patient.

In Brief

Legal Home Study Course

"Legal Problems in the Practice of Medicine," a home-study course, is being offered as a joint project by the AMA and the University of Chicago. Not intended to make lawyers out of doctors, the course is geared to the busy physician who seeks an understanding of the law as it affects him in his day to day work. Tuition is $35; text and selected reading materials will be purchased by the student himself (approximately $25); completed assignments may be mailed in by the registrant at his convenience but the course must be completed within one year. The course is also adaptable for group study—one member submitting an enrollment, paying tuition fee and advising the home-study department of the group enrollment. Extra copies of the syllabus for group members may be purchased at cost by the registrant. For enrollment write: Desk LSE, Home Study Department, University of Chicago, 60th at Dorchester, Chicago 37, Illinois.

"Dat Ole Debil" Nicotine

Serum levels of cholesterol and lipoprotein appear to be higher in smokers than in non-smokers, though the uncomplicated effect of nicotine on these levels is not yet clear, according to *Upjohn Abstract*. Studies show that nicotine is capable of increasing the following: heat production, oxygen consumption, metabolic rate, and blood sugar. It has been shown to possess anticholinesterase activity, and there are reports that ascorbic acid may be depleted to a significant extent.

Cancer Progress

Results of a study indicating that the structure and behavior of human skin epithelial cells are governed by their connective tissue environment have been released by the National Cancer Institute. Skin epithelial cells from 11 patients—9 who had skin cancer, one with mild psoriasis and one with no skin disorder—were transplanted with and without their connective tissue to new places in their hosts. Only when the connective tissue was included did the transplanted cells survive and retain their original characteristics. Otherwise, they either degenerated or developed structural features often resembling epithelium normally resident at the new sight.

Openings In Air National Guard

The Delaware Air National Guard is in the process of activating a new unit, the 166th USAF Dispensary. It will provide four openings for professional personnel with salaries as follows:

Lt. Col (including flight pay)	$2,576
Major (including flight pay)	$2,304
Major	$1,135
Captain	$1,074

Estimates are based on full participation. It will afford members a chance of seeing the world as the Air National Guard will fly a world-wide support mission for the Armed Forces. Membership places a physician in a draft deferred status.

Begin With "Jin"

At the 10th Annual Meeting of ACOG, the College agreed to pronounce the word "gynecologist" with the first syllable as in "jin."

Anti-Measles Serum

The magnitude of the measles problem, causing several hundred deaths in the United States each year, has prompted a three-day international conference on measles immunization to be held November 7-9 at the NIH, Bethesda, under joint sponsorship of the University of Colorado, National Institute of Allergy and Infectious Diseases, and the Division of Biologic Standards. Attack rate among children in most countries is comparable with ours, however in developing areas where nutrition and modern medical facilities are less optimal, mortality can be significant—reaching at times 10% or more. Measles is a world wide problem.

Generic Drug Names Become A Risk

Passage of legislation requiring pharmaceuticals to be sold under generic names would place public health in jeopardy, warned Theodore G. Klumpp, M.D., president of Winthrop Laboratories. All drugs containing the same active ingredients are not identical, he told the physicians attending the Annual Meeting of the Massachusetts Medical Society. Those manufacturers who have confidence in their products give them brand names. The substitutions of generic names for brand names would have the additional effect of discouraging investment in scientific research.

Personal Glimpses

David J. Reinhardt, M.D., was elected president of the Delaware Heart Association, succeeding Robert L. Dewees, M.D. . . . Eugene R. McNinch, M.D., member of the Public Laws Committee, testified for the Medical Society of Delaware against the bill requiring referenda for fluoridation at a State Senate hearing . . . Otakar J. Pollak, M.D., director, presided at a conference on cardiovascular tissue culture held at the Dover Research Center and delivered a paper on nicotine and cigarette smoke . . . Leonard P. Lang, M.D., spoke to the Delaware Society of Medical Laboratory Technicians . . . Harold Tarrant, M.D., spoke on *Detection and Education as a Year Around Program;* David Levitsky, M.D., spoke on *Diets for Juveniles;* Leonard Tucker, M.D., spoke on *How to Regulate the Diabetic Diet in Illness* at a meeting of the lay society of the Delaware Diabetes Association at the Academy of Medicine . . . Floyd I. Hudson, M.D., welcomed the audience to the Nursing Home Institute Program; Arthur J. Heather, M.D., spoke on *Rehabilitation* and A. J. Morris, M.D., spoke on the topic, *What do Doctors Expect of Nursing Homes* . . . James Beebe, Sr., M.D., was written up in the Wilmington Morning News on the occasion of his 80th birthday, spotlighting his contribution to Lewes as a physician and a man . . . Elizabeth Miller, M.D., was guest speaker at the Aldersgate Methodist Church. Topic: *My Sojourn in Nepal as a Medical Missionary* . . . Douglas W. MacKelcan, M.D., won the finals in the New Castle County Medical Society Golf Tournament with low net; Drs. Frederick A. Bowdle and Haynes B. Cates tied with high gross . . .

Editorials

THE FIRST STATE —

From time to time this column has been a sounding board for the excellent medicine found in this little state. In the present issue, among several excellent articles, we have two of outstanding merit in that they represent original investigation. The one by Flinn and D'Alonzo is an impartial investigation of Lipoic Acid as a form of treatment for diabetes. Their investigation and their conclusions are fair and conservative. They fully realize that the dose employed may have been too small but, on the other hand, they are well aware of the fact that larger doses may cause toxic symptoms.

The article by Ravens and his colleagues is a reflection of the excellent neuro-surgical coverage that we are fortunate enough to have here in the State of Delaware.

UNCLE JOE —

The twenty-fifth anniversary of graduation from medical school is a unique milestone in one's professional life. One usually goes back to this reunion to see how his classmates have aged while he has remained exactly the same over this period of time.

Everything seems to have increased at a Twenty-fifth Reunion except the hair and the teeth. The weight, waistline, bifocals, and verbosity usually have increased tremendously.

At a recent Silver Anniversary, it was sad to see one of our old teachers sitting off in the corner. We shall call him Uncle Joe, although his name is not Joseph. We all remembered Uncle Joe as one of our most brilliant teachers. His demonstration of physical findings and his confirmation of these findings by x-ray and other studies left a lasting impression with us and, to no small degree, made all of us better doctors.

Uncle Joe was unhappy because twenty-five years have passed and have found him pushed off into the sidelines. The medical teachers of today do not concentrate upon the bedside teaching, the painstaking history taking or the meticulous physical diagnosis. Today's teachers are from the laboratory and from the ivy towers. They would not dare digitalize a patient without first having circulation time and venous pressure if, in fact, they do not have a cardiac catheterization.

No one doubts that there is a place in modern medicine for the laboratory. Its overemphasis, however, can be just as harmful as its neglect. It is up to the deans of our medical faculties to keep these two important fields—clinical and laboratory medicine—in their true balance and perspective.

Let us hope that someday our sons will have the benefit of the same brilliant teaching that we had from men such as Uncle Joe.

Books

Recent Accessions to the Library of the Delaware Academy of Medicine

BACTERIOLOGY AND IMMUNOLOGY

Gunsalus, I. C. and Stanier, Roger Y. eds.: The Bacteria, Vol. II, The Metabolism, 1961. Academic Press

Zdrodovskii, P. F. and Golinevich, H. M.: The Rickettsial Diseases 1960. Pergamon Press

CARDIOVASCULAR SYSTEM (See also Obstetrics and Gynecology)

Bock, K. D. and Cottier, P. T., eds.: Essential Hypertension, 1960. Springer-Verlag

Daley, Raymond; Goodwin, John F. and Steiner, Robert E. eds.: Clinical Disorders of the Pulmonary Circulation, 1960. Little, Brown and Company

Edwards, Jesse E.: An Atlas of Acquired Diseases of the Heart and Great Vessels, Vol. I, II, III, 1961. Saunders

Gordon, Burgess, L. ed.: Clinical Cardiopulmonary Physiology, 1960. 2nd ed. Grune and Stratton

Harley, H. R. S.: Modern Trends in Cardiac Surgery, 1960. Hoeber

Jacobs, A. L.: Arterial Embolism in the Limbs, 1959. Livingstone

Massie, Edward and Walsh, Thomas J.: Clinical Vectorcardiography and Electrocardiography, 1960. Year Book

Ongley, P. A.; Sprague, Howard B.; Rappaport, M. B.; and Nadas, A. S.: Heart Sounds and Murmurs, 1960. Grune and Stratton

Phibbs, Brendan: Cardiac Arrhythmias, 1961. Mosby

Rushmer, Robert F.: Cardiovascular Dynamics, 1961. Saunders

Taussig, Helen B.: Congenital Malformations of the Heart, 2nd ed., 1960. Harvard University Press

DENTISTRY (See also Psychiatry)

Cheraskin, E.: Diagnostic Stomatology, 1961 McGraw-Hill

Collins, Leon H. and Crane, Martin P.: Internal Medicine in Dental Practice, 1960, 5th ed. Lea and Febiger

Hine, Maynard K.: Review of Dentistry, 3rd ed., 1961. Mosby

Johnston, John F.; Phillips, Ralph W.; and Dykema, Roland W.: Modern Practice in Crown and Bridge Prosthodontics, 1960. Saunders

Silverman, Sidney I.: Oral Physiology, 1961. Mosby

DERMATOLOGY

Pillsbury, Donald M.; Shelley, Walter B. and Kligman, Albert M.: A Manual of Cutaneous Medicine, 1961. Saunders

Sulzberger, Marion B.; Wolf, Jack and Witten, Victor H.: Dermatology, Diagnosis and Treatment, 2nd ed., 1961. Year Book

ENDOCRINOLOGY AND METABOLISM

Ciba Foundation: Metabolic Effects of Adrenal Hormones, 1960. Little, Brown and Company

Ciba Foundation: Adrenergic Mechanisms, 1960. Little, Brown and Company

Monograph on Diabetes, 1960. Upjohn Company

GASTROINTESTINAL SYSTEM

Jones, F. Avery and Gummer, J. W. P.: Clinical Gastroenterology, 1960. Thomas

Keele, Kenneth D. and Matheson, Norman M.: Intra-Abdominal Crises, 1961. Butterworth

HEMATOLOGY

Henry Ford Hospital International Symposium: Blood Platelets, 1961. Little, Brown and Company

INFECTIOUS DISEASES

The Study of Influenza, 1960. U.S. Department of Health, Education and Welfare

MEDICINE (see also Dermatology, Dentistry, Urogenital System)

Brahdy, Leopold: Disease and Injury, 1961. Lippincott

Jones, Mary S.: An Approach to Occupational Therapy, 1960. Butterworth

Morgagni, John Baptist: The Seats and Causes of Diseases, 1960. Vol. 1, 2 and 3. Hafner

MISCELLANEOUS

Armstrong, Harry G.: Aero-Space Medicine, 1961. Williams and Wilkins

Garland, Joseph and Stokes, Joseph, III: The Choice of a Medical Career, 1961. Lippincott

McFadden, Charles J.: Medical Ethics, 5th ed., 1961. Davis

Nagan, Peter S.: Medical Almanac, 1961-62 Saunders

Sells, S. B. and Berry, Charles A., eds.: Human Factors in Jet and Space Medicine, 1961. Ronald Press

Stern, Curt: Principles of Human Genetics, 1960, 2nd ed. W. H. Freeman and Company

Voino-Yasenetskii, A. V.: Evolutionary Regularities as Reflected in the Epileptiform Reaction of Animals to High Partial Oxygen Pressure, 1958. Academy of Sciences of U.S.S.R.

(To be continued)

Auxiliary Affairs

MESSAGE FROM OUR PRESIDENT

The Woman's Auxiliary to the Medical Society of Delaware is proud of its work in health careers.

The committee arranged programs for the Rotary Club of Wilmington and the Lions Club of Milford. As a result of these programs the Rotary Club financed eight nursing awards and one in medical technology, while the Lions Club granted two nursing awards. Members of the committee on health careers did all the processing of applicants for scholarships given by these organizations. The selection of recipients was left entirely in their hands.

There has been excellent newspaper coverage following programs planned and arranged by this committee for service groups. Last year the chairman was guest speaker at the Rotary Club and, as a result of the newspaper publicity, the auxiliary was approached by representatives of an educational television channel to arrange periodic programs. This channel is expected to start programming sometime in the next year. With the advice of the advisory board of the Medical Society of Delaware, we consented to arrange and organize such a program.

Another very important project of our auxiliary is working on medical legislation. This spring the entire state has been concerned with "Operation Coffee Cup." Each member of the Auxiliary has been asked to invite a small group of her friends to hear a record by Ronald Reagan. He has made this record to state his views on medical legislation. We hope to give our friends a more thorough understanding of current legislation before Congress. If all our members and their friends would write their senators and congressman, perhaps they can be persuaded to try the Kerr-Mills bill before passing other medical legislation.

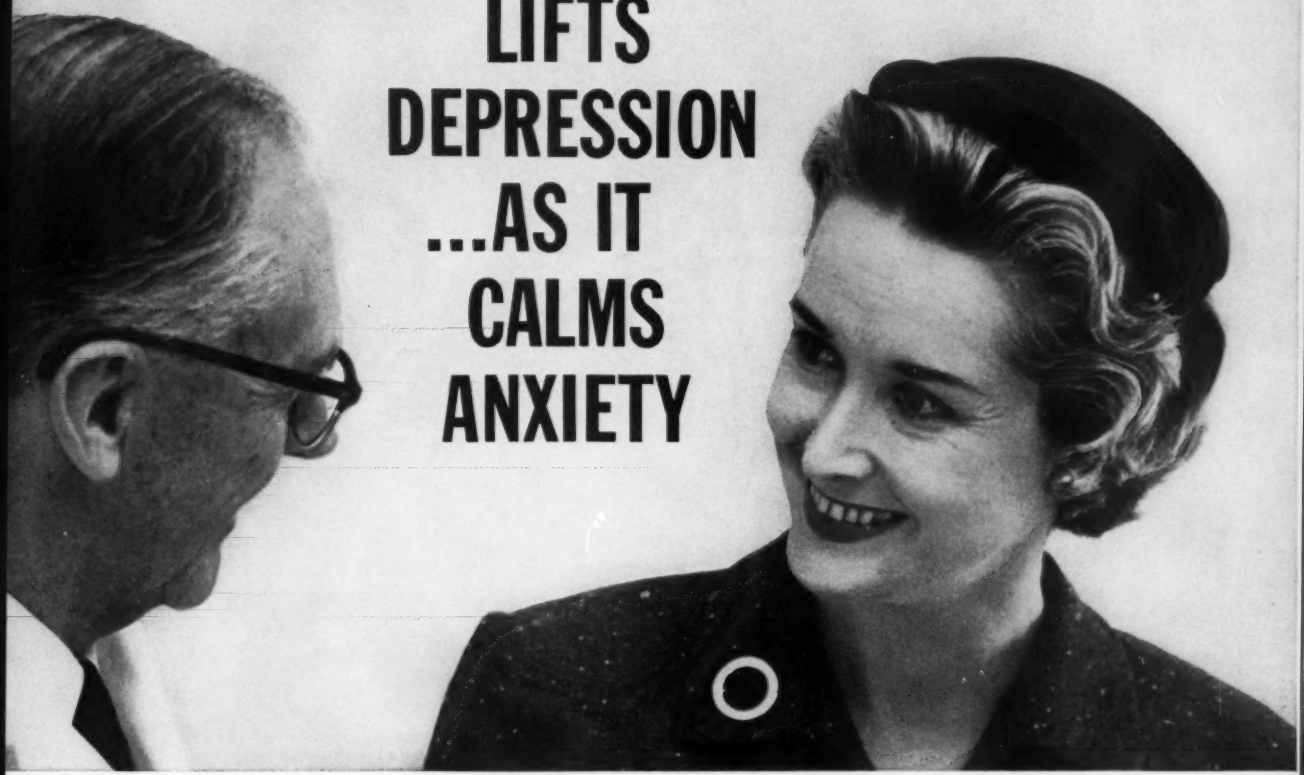
It has been a pleasure to work with all my committee members and the county auxiliaries. Our Auxiliary has important contributions to make in several fields; I have been able to mention only two of particular concern. I am looking forward to working with everyone for the remainder of my term.

Mrs. J. Leland Fox

NURSES WITH LEADERSHIP POTENTIAL

The NLN Fellowship Program provides funds to subsidize programs of advanced study for nurses of proven ability. Fellowships are awarded to qualified applicants irrespective of race, creed, sex, or national origin. Eligibility requirements are: 1. Freedom to pursue a full-time program of master's or post-master's degree study. 2. Acceptance by a recognized university. 3. United States citizenship or first papers. For particulars, contact National League for Nursing, 10 Columbus Circle, N.Y. 19, N.Y.

LIFTS DEPRESSION ...AS IT CALMS ANXIETY



"I feel like my old self again!" Thanks to your balanced Deprol therapy, her depression has lifted and her mood has brightened up – while her anxiety and tension have been calmed down. She sleeps better, eats better, and normal drive and interest have replaced her emotional fatigue.

Brightens up the mood, brings down tension

Deprol's balanced action avoids "seesaw" effects of energizers and amphetamines. While energizers and amphetamines may stimulate the patient – *they often aggravate anxiety and tension.*

And although amphetamine-barbiturate combinations may counteract excessive stimulation – *they often deepen depression and emotional fatigue.*

These "seesaw" effects are avoided with Deprol. It lifts depression as it calms anxiety – a balanced action that brightens up the mood, brings down tension, and relieves insomnia, anorexia and emotional fatigue.

Acts rapidly – you see improvement in a few days. Unlike the delayed action of most other antidepressant drugs, which may take two to six weeks to bring results, Deprol relieves the patient quickly – *often within a few days.* Thus, the expense to the patient of long-term drug therapy can be avoided.

Acts safely – no danger of liver or blood damage. Deprol does not cause liver toxicity, anemia, hypotension, psychotic reactions or changes in sexual function – frequently reported with other drugs.

▲Deprol▲®

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be gradually increased up to 3 tablets q.i.d.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

CD-4524 WALLACE LABORATORIES / *Cranbury, N. J.*

Available only to physicians for their distribution—

Complete Cholesterol Depressant Menus and Recipe Book

A new, authoritative patient-aid . . . for professional distribution only

Now available for use in your practice from The Wesson People . . . easy-to-use manual of 40 pages, including all necessary diet instructions . . . menus, recipes, shopping and cooking guidance . . . all worked out for you . . . so arranged and printed that you have only to check the desired daily calorie level before giving the book to your patient.

You will find this book invaluable for treating patients with elevated serum cholesterol.

Complete menus for 10 days enable you to prescribe diets which are appetizing, nutritiously adequate and which can exert cholesterol depressant activity. Special attention has been given to constructing the menu patterns so that they adhere as closely as permissible to the patient's normal eating habits.

NRC Standards fulfilled. Each menu has been calculated to provide the proper daily allowance of proteins, vitamins and other nutrients as recommended by the Food and Nutrition Board of the National Research Council.

Weight control is achieved as each day's menu is given at 3 calorie levels—1200, 1800 and 2600 calories. You prescribe the level most desirable and modify as desired.

Variety and appetite appeal for patient are built into the menu plan to an extent not previously accomplished. Alternate choices for main dishes minimize monotony, encourage the patient to follow closely the menu plan you specify.

Complete recipes—65 in all—are included to assure that the specified menus provide prescribed levels of calories, the pre-determined ratio of poly-unsaturated to saturated fat, plus essential nutrients.

Dietary fat is controlled so that approximately 36% of the total calories are derived from fat and at least 40% of these fat calories are from poly-unsaturated components (linoleates) as found in pure vegetable oil. The replacement of saturated dietary fat by this percentage of poly-unsaturated fat has been found in clinical studies most effective in the reduction of serum cholesterol and in its maintenance at desirable levels. More liberal menus are provided for maintenance after the patient's progress indicates that desired therapeutic results have been accomplished.

Family meal preparation is simplified. The menus are planned around favorite foods having wide appetite appeal for all members of the household. Patients can entertain in comfort—enjoy cakes, cookies, snacks, prepared with recipes which meet medical requirements.

A high degree of satiety is achieved even at the lower calorie levels, because Wesson provides an unexcelled source of concentrated, slow-burning food energy.

Adaptable for use with diabetics. Carbohydrates have been calculated to fall within the acceptable range for patients to whom a diet planned for diabetes is important. Calories, which must be supplied from fat when the carbohydrate intake is limited, are provided by desirable poly-unsaturated vegetable oil.

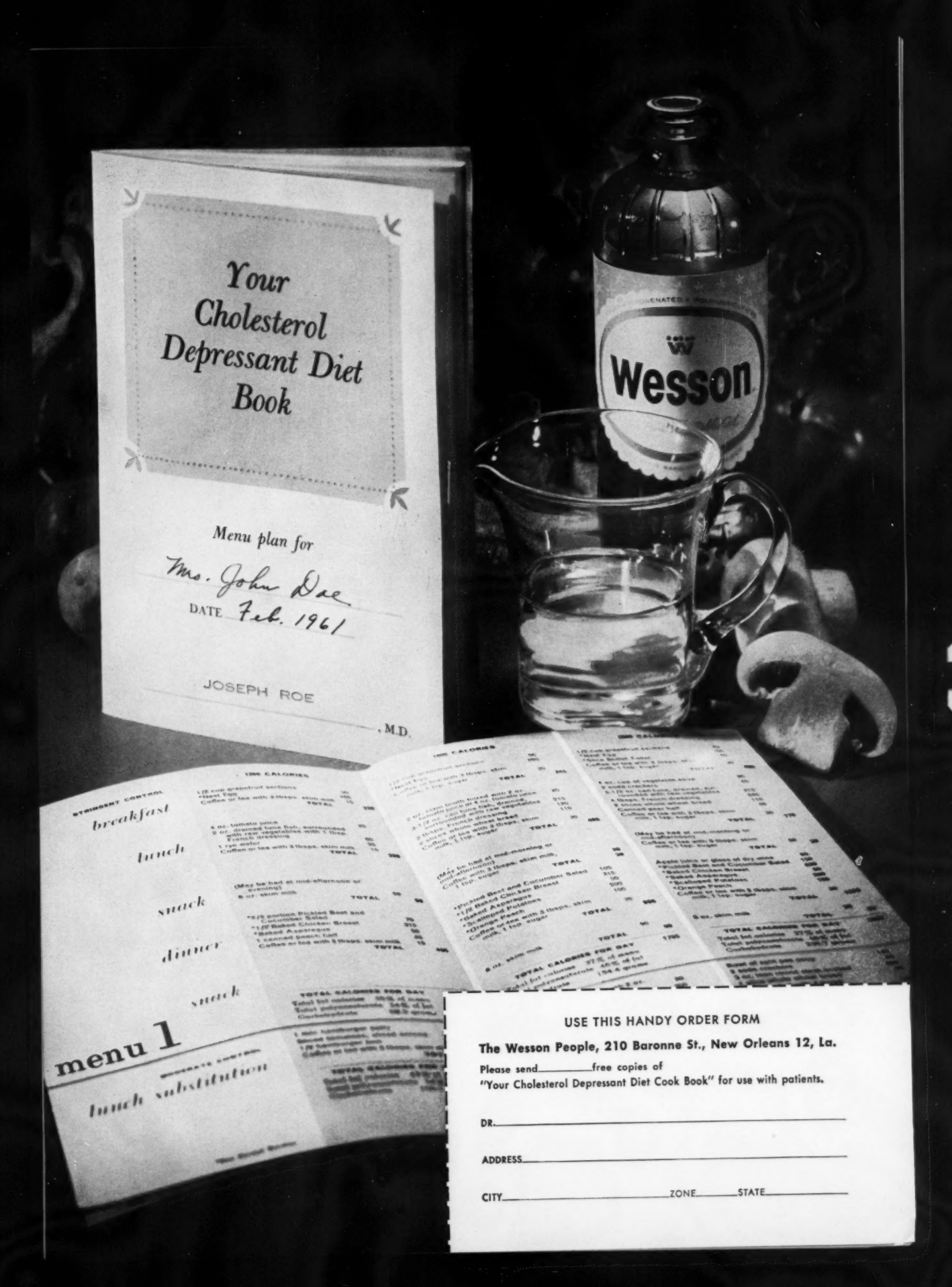
WESSON'S IMPORTANT CONSTITUENTS

Wesson is 100% cottonseed oil—winterized and of selected quality

Linoleic acid glycerides (poly-unsaturated)	50-55%
Oleic acid glycerides (mono-unsaturated)	16-20%
Palmitic, stearic and myristic glycerides (saturated)	25-30%
Phytosterol (Predominantly beta sitosterol)	0.3-0.5%
Total tocopherols	0.09-0.12%

Never hydrogenated—completely salt free

Poly-unsaturated Wesson is unsurpassed by any readily available brand, where a vegetable (salad) oil is medically recommended for a cholesterol depressant regimen.



LOGICAL NEW DERMATOLOGICAL HELPS

solve the mystery of Acne Therapy

Brāsivol has a gentle abrasive action that attacks the acne lesion simply and directly. It maintains the mild desquamation so essential to the successful acne regime. Helps open plugged pores, reduce pustules and blackheads, control oiliness. Helps minimize postacne scars. The patient simply applies Brāsivol abrasive cleanser 2 or 3 times daily, and rinses. Ritual helps relieve urge to squeeze pimples. Cooperation is enhanced because results are readily seen and felt. Safety and success are supported in over 10 years of clinical studies on thousands of acne cases. Brāsivol (pat. pend.) contains precisely sized abrasive particles (fused aluminum oxide) and hexachlorophene 1%, in a detergent and drying base. Compatible with other therapeutic measures.

Write for starter samples and literature

STIEFEL®

LOGICAL DERMATOLOGICALS—since 1847

Oak Hill, New York

CANADIAN REPRESENTATIVE:
WINLEY-MORRIS CO., LTD., Montreal 29, Quebec

Brāsivol Fine *Brāsivol Medium* *Brāsivol Rough*

Brāsivol is supplied in 3 abrasive grades, permitting gradual intensification of abrasive action as the acne improves. Also, Brāsivol Base (abrasive free) now available for acute inflammatory cases.

Jars of Brāsivol Base 5 oz.; Brāsivol Fine 5¾ oz.; Brāsivol Medium 6¼ oz.; Brāsivol Rough 7 oz.

Brāsivol®

ABRASION THERAPY FOR ACNE

in certain other countries Brāsivol is available as DENCO-BRAS™

REFERENCES:
SAPERSTEIN, R. B.: Treatment of Acne with Long Term Continuous Abrasion. A.M.A. Archives of Derm. 81: 601, April 1960.
REES, R. B.; BENNETT, J. H.; GREENLEE, M. R.: Newer Drug Treatment in Dermatology, Cal. Med., 91:1, July 1959.
SULZBERGER, M. B. & WITTEN, V. H.: The Management of Acne Today. Med. Clinics of No. America, 43:3, May 1959.

REFER TO PDR

in the wide middle region of pain

Percodan

(Salts of Dihydrohydroxycodeinone and Homatropine, plus APC)

TABLETS

fills the gap between mild oral and potent parenteral analgesics[1-7]

- **acts in 5-15 minutes**
- **relief usually lasts 6 hours or longer**
- **toleration excellent... constipation rare**
- **sleep uninterrupted by pain**

Each Percodan* Tablet contains 4.50 mg. dihydrohydroxycodeinone HCl, 0.38 mg. dihydrohydroxycodeinone terephthalate (warning: may be habit-forming), 0.38 mg. homatropine terephthalate, 224 mg. acetylsalicylic acid, 160 mg. acetophenetidin, and 32 mg. caffeine.

for fast and thorough pain relief

AVERAGE ADULT DOSE
1 tablet every 6 hours. May be habit-forming. Federal law permits oral prescription.

Also Available
For greater flexibility in dosage — Percodan*-Demi: The complete Percodan formula, but with only half the amount of salts of dihydrohydroxycodeinone and homatropine.

1. Blank, P., and Boas, H.: Improved analgesia for moderate pain, Ann. West. Med. & Surg. 6:376, 1952. 2. Bonica, J. J., et al.: The management of postpartum pain with dihydrohydroxycodeinone (Percodan): Evaluation with codeine and placebo, West. J. Surg. 65:84, 1957. 3. Cass, L. J., and Frederick, W. S.: A controlled study in pain relief, M. Times 84:1318, 1956. 4. Chasko, W. J.: Pain-free dental surgery: Postoperative extension of the pain-free state, J. Distrct of Columbia Dent. Soc. 31:3, No. 5, 1956. 5. Cozen, L.: Office Orthopedics, ed. 2, Philadelphia, Lea & Febiger, 1953, pp. 120, 138, 145, 156, 234. 6. Nicolson, W. P., Jr., and Skandalakis, J. E.: Control of postoperative pain, J.M.A. Georgia 46:471, 1957. 7. Piper, C. E., and Nicklas, F. W.: Percodan for pain in industrial practice, Indust. Med. 23:510, 1954; abstracted, Clin. Med. 3:1008, 1956, Current M. Digest 22:135, No. 3, 1955.

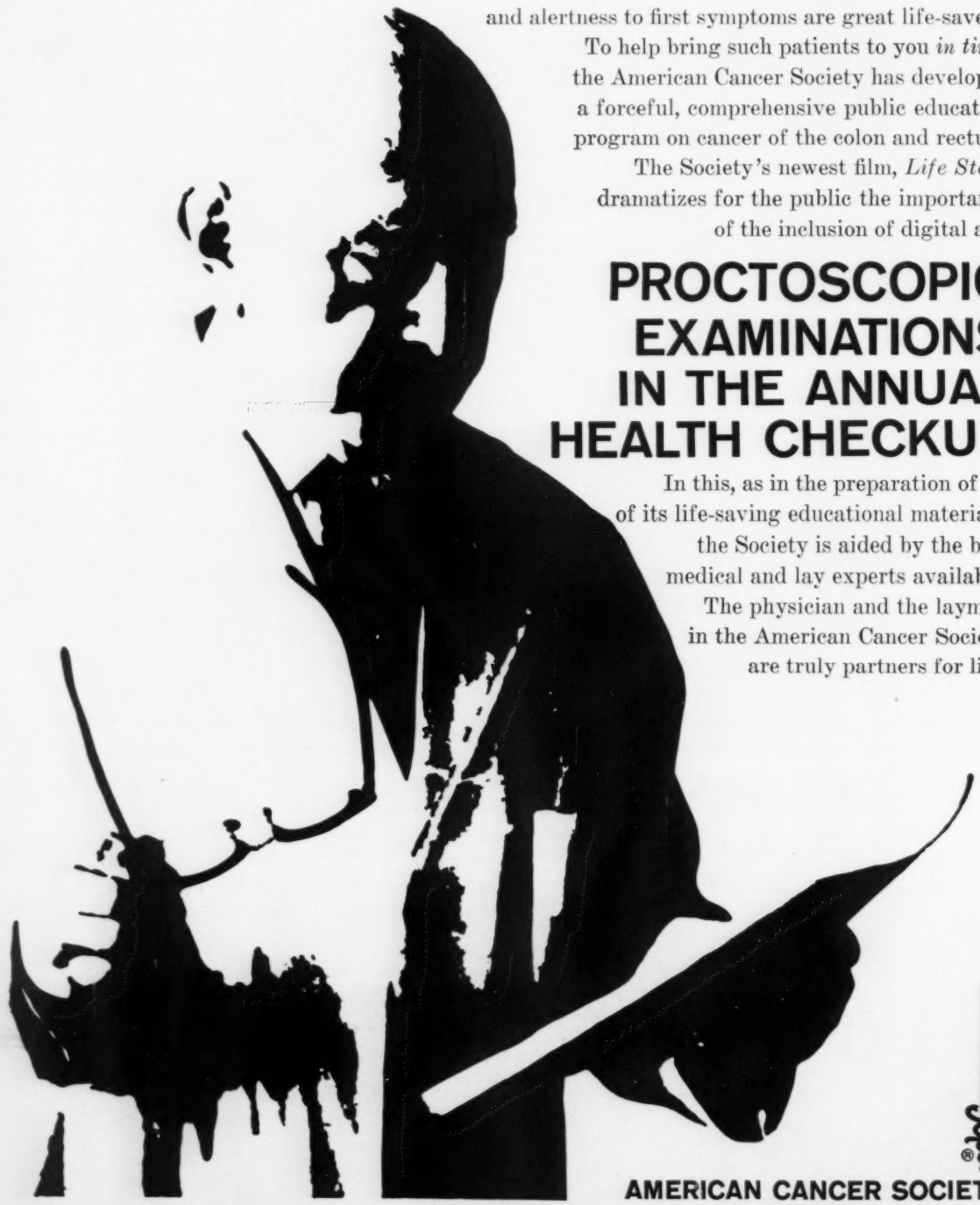
Endo® ENDO LABORATORIES
Richmond Hill 18, New York

*U.S. Pats. 2,628,185 and 2,907,768

In 1961, you, the nation's physicians, will diagnose an estimated 70,000 cases of cancer of the colon and rectum. Although potentially this is a highly curable cancer, each year more than two thirds of such patients die of the disease. Thousands are lost needlessly. They could be saved by proper medical treatment of the disease, found by annual examination, in its presymptomatic and most curable stage. The regular health checkup and alertness to first symptoms are great life-savers. To help bring such patients to you *in time*, the American Cancer Society has developed a forceful, comprehensive public education program on cancer of the colon and rectum. The Society's newest film, *Life Story* dramatizes for the public the importance of the inclusion of digital and

PROCTOSCOPIC EXAMINATIONS IN THE ANNUAL HEALTH CHECKUP.

In this, as in the preparation of all of its life-saving educational materials, the Society is aided by the best medical and lay experts available. The physician and the layman in the American Cancer Society are truly partners for life.



AMERICAN CANCER SOCIETY

Trademarked drugs . . .

or "drugs anonymous"?

In the field of medicine, as almost everywhere else in a free economy, the trademark concept has evolved over the years. As with most human institutions, there are some who may not consider it ideal; but it has brought about three signal benefits:

To the physician it gives assurance of quality in the drugs he prescribes—assurance backed by the biggest asset of the maker, his reputation.

To the manufacturer it gives one of the greatest possible incentives to produce new and better curative agents.

To the pharmacist it gives preparations which he can dispense with confidence.

If trademarks are done away with, a whole new setup must be created:

1. An enormously expanded, expensive system of government quality control.

2. A new system of generic nomenclature which would magically turn out names not only rememberably simple, but also conforming to the principles of complex chemical terminology.

3. Something new to fill the gap left by the elimination of the trademark incentive to produce new and better drugs.

The American system has been pre-eminent in producing and distributing good medicines. Above all it has been successful in creating new advances in therapy. In a dubious effort to provide cheaper medicines by abolishing the trade names upon which the responsible makers stake their reputations, let us beware of sacrificing this success.

This message is brought to you on behalf of the producers of prescription drugs to help you answer your patients' questions on this current medical topic. For additional information, please write **Pharmaceutical Manufacturers Association,** *1411 K Street, N. W., Washington 5, D.C.*

earlier detection of peripheral vascular disease key to improved therapeutic response

In practically all peripheral vascular disease cases where marked occlusion with severe ulceration or frank gangrene has not developed, patients can be assured that excellent treatment is available and many symptoms can be relieved.[1] Routine palpation of peripheral pulses[2] and performance of clinical tests for peripheral arterial disease[3] will help earlier diagnosis. Consequently treatment can be instituted sooner, improving likelihood of a favorable response to therapy.

VASODĪLAN®

Isoxsuprine hydrochloride, Mead Johnson

myo-  -vascular relaxant

increases deep peripheral circulation by direct action ...without troublesome side effects

VASODĪLAN'S record of safety and effectiveness in the management of peripheral vascular disease has been established clinically.[4-6] Clarkson and Le Pere report: With strictly a clinical office approach, isoxsuprine [VASODĪLAN] was used in the treatment of 100 patients with peripheral vascular disorders. Definite clinical improvement was obtained in 89 per cent of these patients."[5] They further state: "In particular, the symptoms of pain, cramping, numbness, and cold were consistently relieved."[5]

Contraindications – There are no known contraindications to oral administration of VASODĪLAN in recommended doses.

Cautions – VASODĪLAN should not be given immediately postpartum or in the presence of arterial bleeding. Parenteral administration is not recommended in the presence of hypotension or tachycardia. Intravenous administration is not recommended because of the increased likelihood of side effects.

Side effects – Few side effects occur when given in recommended doses. Occasional palpitation and dizziness can usually be controlled by dosage adjustment. Single intramuscular doses of 10 mg. or more may result in hypotension or tachycardia.

Dosage and administration – Oral – 10 to 20 mg. (1 to 2 tablets) t.i.d. or q.i.d.; I.M. – 5 to 10 mg. b.i.d. or t.i.d.

Supplied – 10 mg. tablets, bottles of 100; 2 cc. ampuls (5 mg./cc.) for intramuscular use, boxes of 6.

For complete details on indications, dosage, administration and clinical background of VASODĪLAN, see the brochure of this product available on request from Mead Johnson Laboratories, Evansville 21, Indiana.

References: (1) Lieberman, J. S.: GP *21*:133-143 (March) 1960. (2) DeWeese, J. A.: New England J. Med. *262*:1214-1217 (June 16) 1960. (3) Winsor, T.: Peripheral Vascular Diseases: An Objective Approach, Springfield, Illinois, Charles C Thomas, 1959, pp. 457-458. (4) Kaindl, F.; Samuels, S. S.; Selman, D., and Shaftel, H.: Angiology *10*:185-192 (Aug.) 1959. (5) Clarkson, I. S., and Le Pere, D. M.: Angiology *11*:190-192 (June) 1960. (6) Samuels, S. S., and Shaftel, H. E.: J.A.M.A. *17*:142-145 (Sept. 12) 1959.

57861

Mead Johnson Laboratories

Symbol of service in medicine